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CONTENTS

Pathology PAGES
b. *Physiological (concluded)* 25–26
c. *Chemical* 26–28
d. *Serological (tuberculin, allergy, immunity, etc.)* 28–34
e. *Bacillary (tubercle and related bacilli)* 34–42
Diagnosis (*X-ray, tuberculin, serological, etc.*) 42–48

Tuberculous Plasma Affecting Fibroblasts.—In this report the effect of plasma from rabbits with tuberculosis on normal fibroblasts *in vitro* is described. Rabbits were inoculated intravenously with 0.1 mgm. of bovine tubercle bacilli (B1), a litter-mate serving as a control in each instance. The cells used for testing the influence of the plasma were so called fibroblasts grown from the testes of adolescent rabbits. These were obtained by planting the testes in a medium consisting of heparinized rabbit plasma and rabbit embryonic extract. Subcultures were made later and some of the same stock served as a control from each transplant. The blood was allowed to drop from the incised ear-vein into tubes containing heparin to obtain the test plasma. This was added to the flasks in small dosage, one of each pair receiving tuberculous plasma and the other normal rabbit plasma. The influence of the abnormal plasma is expressed by the ratio $\frac{\text{Tuberculous plasma}}{\text{Normal plasma}}$. When this is distinctly less than 1 it indicates that growth-depressing influences in the environment predominated, and, when more than 1, that growth-stimulating factors were dominant. The average indices obtained with plasma from tuberculous rabbits in the first 3 months of the disease were below 1, while most of those from rabbits having had tuberculosis 6 to 11 months were above 1. These two effects roughly parallel the diphasic nature of tuberculosis in rabbits. With one or two exceptions all of the animals used in the experiment passed into the chronic stage of the disease. The probable explanation of the depressing influence on fibroblastic growth observed with plasma in the early period of tuberculosis is the presence of an excess of lipoids in these plasmas. There is a period of leucopoenia at this time followed by a stage of distinct leucocytosis later in the disease. The growth-stimulating substances occurring in the second phase of the disease may have some relation to the leucocytosis. It is of interest that the stage of tuberculosis in which there is a distinct tendency for the animal to wall off the lesions with a fibrous capsule is also characterized by the presence in its plasma of substances which stimulate the growth of fibroblasts to an unusual degree.—*Varying Influence of Tuberculous Rabbit Plasma on the Growth of Fibroblasts in Vitro, H. F. Swift, J. K. Moen & E. Vaubel, J. Exper. Med., August 1, 1934, lx, 149.*—(*J. S. W.*)

Blood in Chronic Respiratory Diseases.—Comparisons were made of normal blood and plasma volumes in 25 normal male subjects whose average age was 26 years, with the corresponding volumes in 16 cases of pulmonary emphysema and 14 cases of pulmonary fibrosis. These volume determinations were made in conjunction with clinical observations and measurements of pulmonary capacity and gas content of the arterial blood. Normal mean plasma volumes were determined by the method of injecting intravenously 4 mgm. per kg. body weight of a 1.5 per cent solution of brilliant vital-red, freshly prepared and filtered. Subsequent volumes were calculated according to the formula of Hooper, Smith, Belt and Whipple. The authors found marked variations in values for total blood volume

and its components in the group of normal subjects. There being a significant correlation between volume of blood and body weight, this basis was used to calculate expected values for the blood volume in pathological cases. Of these, 16 had emphysema associated with chronic bronchitis, bronchiectasis or asthma, with cyanosis and clubbing of the fingers in a large proportion; in 10 of the 14 cases of fibrosis, the disease was suspected to be silicosis, the aetiology of the fibrosis in the remaining cases not being known. In the emphysema group no important alterations from the normal were found in the plasma, blood and cell volume or total circulating haemoglobin estimations. In the fibrosis cases mean values for the cell volume and total haemoglobin were definitely increased, due to marked alterations in three cases, and not a consistent increase. The plasma volume was normal. In the three markedly altered cases there was found a hydraemic plethora, and the arterial oxygen saturation was markedly decreased. In two of these cases signs and symptoms, with the exception of an enlarged spleen, were identical with those of so-called "primary" polycythaemia. In the groups studied there was no correlation between severity and duration of symptoms and the increase in blood volume, nor was there correlation between alterations in the blood volume and changes in the pulmonary capacity. Mean values per gram of haemoglobin and the red cell volume per 100 cc. of blood were within normal limits in the emphysema cases, but the fibrosis cases showed a moderate increase. Mean values for the red cell count were within normal limits in both groups of cases. —*Study of the Blood in Chronic Respiratory Diseases, with Special Reference to the Volume of the Blood, N. L. Kaltreider, A. Hurtado & W. D. W. Brooks, Jour. Clin. Invest., November, 1934, xiii, 999.*—(*G. L. L.*)

Function of Lung as "Blood Depot."—Bancroft stated in 1923 that to be a blood depot an organ must clearly contain important quantities of blood which are unnecessary or at least temporarily unnecessary for its own metabolism and which can be transferred to other organs in order to meet their needs. On the basis of this definition, the lung must be considered to be a blood depot. The experimentally proved fact that the lung is able to store much blood and to deliver it in a short period of time leads to the conception that the previous statement can be justified. Comparative experiments on the splenic and pulmonary circulations reveal some findings concerning a better knowledge of the biological importance of the various blood depots in connection with the general circulation. The mechanism of a blood depot apparently lies not in the pulmonary artery but more in the smaller vessels of the lung circuit.—*Die Lunge ein Blutdepot, M. Hochrein & C. J. Keller, Klin. Wchnschr., September 29, 1934, xiii, 1383.*—(*F. G. K.*)

Capillary Blood-Flow in Lung.—The following conclusions are drawn from direct microscopical observation of capillaries in the cat's lung, without opening of the pleural cavity; the number of pulmonary arterioles and capillaries through which the blood circulates at a given time is subject to spontaneous variation and may be influenced by certain drugs. In the arterioles there exists a certain intermittence of the blood-flow. The number of capillaries through which blood flows at any given time is apparently only a small fraction of the total number of capillaries available. Both the velocity of the blood-flow and the cellular composition of the blood vary in capillaries arising from the same arteriole. No evidence of contraction of capillary walls was observed, and hence it is concluded that the variation in capillary blood flow is caused by changes in the arterioles.—*The Normal Behavior of the Pulmonary Blood Vessels with Observations on the Intermittence of the Flow of Blood in the Arterioles and Capillaries, J. T. Wearn, A. C. Ernstene, A. W. Bromer, J. S. Barr, W. J. German & L. J. Zschiesche, Am. J. Physiol., August, 1934, c, 236.*—(*M. P.*)

Carbohydrate Metabolism in Tuberculosis.—The blood-sugar level is within normal limits in patients with minimal or moderately advanced lesions. In far-advanced patients, there is a tendency toward hyperglycaemia. In glucose-tolerance tests, tuberculous patients show a diminished sugar tolerance. Adrenalin injection shows that the glycogenic function of the liver is impaired and that there is a depletion of the glycogen depots. Studies with insulin administration indicate an insufficiency of the adrenal system in tuberculous patients.—*Der Kohlenhydratstoffwechsel bei Tuberkulösen, R. J. Drabkina, Beitr. Klin. Tuberk., September, 1934, lxxxv, 295.*—(*M. P.*)

Oxidation-Reduction Studies with Phthiocol.—Phthiocol, 2-methyl-3-hydroxy-1,4-naphthoquinone, a pigment isolated from the human-type tubercle bacillus, is the oxidant of a reversible oxidation-reduction system, with a normal potential at 30° of 0.2987 volt, which is among the lowest reported for systems of biological origin. The dissociation constant for the oxidant was $K_0 = 8.32 \times 10^{-6}$, and for the reductant $K_1 = 1.26 \times 10^{-9}$ and $K_{r2} = 2.88 \times 10^{-12}$.

Phthiocol is suitable for use as an oxidation-reduction indicator at pH values more alkaline than 6.0. The relation of this system to other naturally occurring systems, whose oxidants are also hydroxynaphthoquinones, is discussed.—*Studies on Oxidation-Reduction. XXI. Phthiocol, the Pigment of the Human Tubercle Bacillus, E. G. Ball, J. Biol. Chem., September, 1934, cvi, 515.—(F. B. S.)*

Experimentally Induced Deposition of Calcium in Lung.—Previous work on gelatinothorax is referred to, using a preparation of gelatin-acriflavine in place of oil. The Bridge of Weir Sanatorium, Renfrewshire, Scotland, has since adopted gelatinothorax as a routine method in cases presenting tuberculous empyema or pleural effusion, with distinct benefit in most cases. The medium mixes well and maintains collapse reasonably well. Questions of its mode of action, absorption and elimination remained to be answered. It is known that a pathological serosa has its powers of absorption more or less impaired. *Experimental series 1:* Five rabbits were selected and injected intrapulmonarily on the right side with a small dose of human tubercle-bacillus suspension from a year-old primary culture, and again 16 days later with a dose from a fresh 3-plus sputum, each getting 0.5 cc. of the antiforminized sediment in saline solution. Two of the 5 were used as controls, 3 were given a minimal artificial pneumothorax, after which they received gelatin-acriflavine at frequent intervals into the pleura over a period of one to two months. None of the rabbits showed marked tuberculous lesions, probably owing to resistance to the human type, but there was a noteworthy production of hyaline connective tissue in the injected animals, confined to the pleural and subpleural tissues. *Experimental series 2:* Calcium chloride was incorporated in the medium (5 per cent strength), and a healthy rabbit and series of tubercle-infected guinea pigs (intrapulmonary) were injected intrapleurally at frequent intervals. Doubtless many or most of the injections were intrapulmonary as well. Calcification and hyaline changes were almost invariably found in the lesions produced. *Experimental series 3:* Intrapulmonary injections of the G. A. C. C. medium were given 6 healthy rabbits. One died at once and showed a collapsed lung. Another died later showing a collapsed lung, another died accidentally. Giant-cell formation was common, and all but one showed calcification at necropsy. *Experimental series 4:* A series of 20 guinea pigs were injected (intrapulmonary) with a lethal dose of tubercle bacilli and treated with G. A. C. C. in the same way. Then a series of 32 rabbits was used, 22 treated and 10 controls. Ten of the treated died of intercurrent diseases and accidents, some admittedly due to the treatment. Of the others, calcium deposition was almost invariable and fibrosis common on the treated side. It appeared to be demonstrated that rapid calcification could be induced by very small doses of G. A. C. C. The injections must be slow, with a fine needle, with care to avoid blood-vessels. It also appears that hyaline changes are an essential preliminary.—*Induced Deposition of Calcium in Lung Tissue: an Experimental Study, R. A. Hunter & D. Bell, Tubercle, October, 1934, xvi, 1.—(A. P.)*

Calcium Content of Sputum.—The calcium content of sputum is greater in acute than in chronic lesions. Sputa from non-tuberculous lesions contain an average of only about half the amount of calcium of sputa from tuberculous lesions.—*Untersuchungen über den Calciumgehalt des Sputums von Tuberkulösen, S. Puder & T. Herczog, Beitr. Klin. Tuberk., October, 1934, lxxxv, 364.—(M. P.)*

Iron in Tuberculous Foci.—Previous studies by the writer have demonstrated that repeated intravenous injections in tuberculous rabbits of dilute ferric-chloride solution are followed by an accumulation of iron in the tubercles. The course of the disease was found to be retarded, as evidenced by an increase in the survival time and by the less extensive involvement of the lungs of experimental animals as compared with controls that had the disease for the same length of time. When the intravenous ferric-chloride treatment promptly followed subcutaneous injection of the bacilli, the dissemination of the latter from the site of inoculation was retarded. Reinfected rabbits receiving ferric chloride lived over twice as long as the nontreated controls. The present experiments have to do with the combined effect of partial immunity and ferric-chloride administration on the course of experimental tuberculosis. Ten rabbits were inoculated intravenously, each with 0.005 mgm. of a relatively avirulent strain of bovine tubercle bacilli (Cernay). About 6 weeks later each of these animals received subcutaneously in the thigh 0.05 mgm. of a virulent bovine strain (Ravenel). The non-vaccinated group consisted of 10 animals that received the virulent bacilli alone. In 5 of each group, intravenous injections of ferric chloride (0.25 per cent in distilled water) were started immediately and continued for a period of about 4 months. As

a rule about three injections of 6 cc. each of the iron salt were made every week. In the vaccinated group the iron-treated animals survived on an average of 198 days, whereas the untreated animals lived on an average of only 81 days. In the nonvaccinated group the iron-treated animals had an average survival time of 246 days whereas the untreated animals lived 130 days. The two groups were not inoculated with the virulent bacilli simultaneously, nor was the same suspension employed, hence the discrepancy in the survival time of the two groups. The two series can be compared only in regard to the respective differences between the survival time of experimental and control rabbits. As a matter of fact the true average survival time of the iron-treated vaccinated group was greater than 198 days, for two of the animals were killed on the 334th day. The results of the present series of experiments again show definitely that repeated intravenous injections of dilute ferric-chloride solution retard markedly the course of development of tuberculosis in rabbits. Apparently the action of partial immunity induced by a first infection enhances the favorable effects of the iron salt in reinfected animals. The favorable action of the ferric chloride may be the result of several factors. The frequent appearance of intense vascular congestion associated with some fibroblastic proliferation in tuberculous lesions of iron-treated animals suggests the end-stage of a superimposed inflammatory reaction induced by the accumulation of iron in the tubercles. The introduction of this additional synergistic element would enhance the various factors in the tubercle which naturally tend to dispose of the bacilli. Furthermore the frequent deposition within mononuclear phagocytes of an iron-containing pigment, undistinguishable from haemosiderin, may, by activating the cells of the recticuloendothelial system, constitute a factor in the favorable effect of ferric-chloride administration. The cells of this system loaded with the iron-containing pigment may be more readily detached and may thus be disseminated in greater numbers to tuberculous foci.—*The Accumulation of Iron in Tuberculous Areas. IV. The Effect of Ferric Chloride on the Course of Tuberculosis in Reinfected Rabbits, V. Menkin, J. Exper. Med., October 1, 1934, lx, 463.*—(*J. S. W.*)

Constitution of Tuberculostearic Acid.—Tuberculostearic acid, an optically and physiologically inactive saturated liquid fatty acid isolated from the lipoid fractions of the tubercle bacillus, was purified and found to possess the empirical formula $C_{19}H_{38}O_2$. On drastic oxidation of this substance with chromic acid in glacial-acetic acid solution, the two compounds, azelaic acid and methyl n-octyl ketone, were isolated and definitely characterized, indicating that the constitutional formula of the tuberculostearic acid may be 10-methylstearic acid. A synthetic dl-10-methylstearic acid resembled it very closely, but was not identical. The melting points differed by 10°. The prepared solid derivatives differed in crystalline form but possessed identical melting points, densities and refractive indices, and formed the same peculiar lead salt, which was easily soluble in ether but sparingly so in 95 per cent alcohol.—*The Chemistry of the Lipoids of Tubercle Bacilli. XXXIX. The Constitution of Tuberculostearic Acid, M. A. Spielman, J. Biol. Chem., August, 1934, cvi, 87.*—(*F. B. S.*)

Antigenic Chemical Constituents of Tubercle Bacillus.—Tubercle bacilli were thoroughly dried and pulverized in a ball-mill and extracted in epichlorhydrin until the residue lost its acid-fastness completely. The wax extracted in this way was dissolved in alcohol and tested in the complement-fixation reaction with the sera of tuberculous patients. Fixation occurred in isolated instances. The most effective reagent appeared to be the alcoholic extract of the dewaxed bacilli which contained the combined lipoids and not the isolated phosphatides. The reaction was strengthened by the addition of specified amounts of lecithin and the wax extract from the tubercle bacilli. The proteins of the tubercle bacillus tested in the same reaction were *Ertuban*, an extract of living tubercle bacilli with sterile distilled water, and *Tebeprotein*. Both these substances fix complement only in the presence of titrated amounts of lecithin. The polysaccharides of the tubercle bacillus obtained by different methods gave no complement fixation or precipitins, even on the addition of lecithin. The authors call attention to numerous factors which will affect the character and amounts of the various fractions which can be isolated from the tubercle bacillus, such as the medium upon which the bacilli are grown, the solvents used, and the age of the bacillus at the time of extraction. The younger the bacilli the less lipoid they contain.—*Chemischer Aufbau und antigenes Verhalten des Tuberkel Bazillus, F. Klopstock & C. Cattaneo, Ztschr. Immunitäts-forsch., December, 1934, lxxxiv, 34.*—(*M. B. L.*)

Old Tuberculin.—At a Conference under the auspices of the Health Organization of the League of Nations held in Paris in May, 1933, it was decided to investigate with the

tuberculin test, preferably the intracutaneous, the incidence of tuberculous infection among different classes of population in different countries. The use of the same preparation and dosage seemed advisable. Tuberculin, prepared from the growth of the organism on synthetic medium was recommended, with the potency to be assayed in terms of International Standard Old Tuberculin and to be not less than twice this standard. The stability of dilutions was also to be investigated. *Technique of preparation:* The medium employed at the British National Institute for Medical Research was a modification of that of Long, distributed in amounts of 750 cc. in quart bottles, and sterilized by heating to 115°C. for thirty minutes in bottles plugged with antiseptic-treated cotton wool. The strain was a human one, of low virulence for animals, quick growth and of high tuberculin potency. Seed cultures and transplants were made and a portion of the film of a rapidly growing culture not more than ten days old was floated on to the surface of the synthetic medium in a series of about 30 bottles at a time, on their side. After incubation at 37° to 38°C. for twelve weeks, when there should be abundant growth, the bottles are steamed for one hour and the bacillary mass removed by filtration through fine wire gauze. Glycerol is added to make a concentration of 5 per cent and the filtrate concentrated by evaporation on the water-bath to one-tenth its original volume, after which the precipitate is removed by filtration through cellulose padding or Chardin filter paper. Four separate 20-litre batches were separately prepared, then pooled and tested for potency. In an early test, a sample prepared March 20, 1933, and at that time showing more than 2x potency, showed on August 30, 1933 a 1-potency and by October 1st this was practically zero. This was shown by investigation to be caused by the low glycerol content of synthetically prepared tuberculin, which in turn was due to dehydration by phosphorus pentoxide *in vacuo* following storage at low temperatures (−4°C.) causing the samples in question to dry to a scaly solid mass. The presence of the phosphorus pentoxide, in turn, was due to mould contamination, which quickly renders dilutions completely inactive. Glycerol plays an indirect part by acting as a bacteriostatic agent in 50 per cent or higher concentrations. Thereafter sufficient glycerol was added to make the final filtrate contain 50 per cent before evaporation took place and the final product was also tested to ensure this. *Potency and stability tests:* All potency tests were carried out by the intracutaneous method on tuberculous guinea pigs, 0.2 cc. of the test dilutions being injected into one flank of the test-animal, and 0.2 cc. of a similar dilution of International Standard Old Tuberculin at a corresponding site on the other flank. Tests on groups of 3 animals showed the potency of the new standard tuberculin to be between 2 and 3 times that of the International Standard preparation. Regarding the stability of dilutions of Old Tuberculin, statements are conflicting, Jowett and Calmette advocating frequent preparation of fresh dilutions, Parish and Okell finding appreciable deterioration after one month, and Willis noting inconstancy of the higher dilutions, while Fernbach and also Pilcher found dilutions up to 1:100 remarkably stable. One factor not often considered is the pH reaction of the dilution. If an alkaline reaction is guarded against by using containers of special glass, or buffered solutions (boric-borate), the stability and keeping qualities should be enhanced. In the course of the present study dilutions between 1–100 and 1–5000 of both the International Standard Old Tuberculin and the new standard synthetic Old Tuberculin were made up in (1) physiological salt solution, (2) boric-borate-buffer mixture, (3) buffer mixture with 0.02 per cent gelatin added and the reaction adjusted to pH 7.8, and (4) 0.5 per cent phenol in physiological salt solution. Approximately 2.5-cc. quantities of these dilutions were distributed into previously sterilized ampules made of nonalkaline resistance glass, the ampules then being sealed. Some were stored at +2°C., some at room temperature, and some at 37°C. The effect of storage and other treatment was studied by comparing their intracutaneous reactions in guinea pigs (tuberculous-infected) with those produced in similar locations by freshly made dilutions. The effects of heat on both diluted and undiluted tuberculins were also examined. *Summary of results: 1:* Old Tuberculin is remarkably stable. Even autoclaving and prolonged high heat do not deprive either the original or the dilutions of more than one-half their original activity. *2:* The new standard preparation from synthetic media is at least as stable as the International Standard Old Tuberculin. *3:* Storage at 37°C. for 121 days caused about a 50 per cent loss of activity in the buffer mixtures and some of the saline dilutions, but less in others. Dilutions prepared from synthetic media lost less than those of the International Standard Old Tuberculin. *4:* Storage at room temperature and at +2°C. for 121 days resulted in some loss of activity in the I. S. Old Tuberculin dilutions in saline solution but the buffer-mixture dilutions containing gelatin showed no detectable

loss. *5:* Dilutions of both tuberculins in 0.5 per cent phenol in saline solution lost approximately one-half their activity on being heated to 110°C. for thirty minutes and 100°C. for one hour. Storage at 37°C. for 53 days resulted in no loss of activity in the dilutions of tuberculin from synthetic media but some loss in the dilutions of I. S. Old Tuberculin. Neither lost any activity after storage at room temperature or at +2°C. for 53 days. *6:* The usually employed diluents seem as satisfactory as the specially buffered ones.—*The Preparation of Old Tuberculin by the Use of Synthetic Media, with Observations on its Properties and Stability, S. R. Douglas & P. Hartley, Tubercle, December, 1934, xvi, 105.*—(*A. P.*)

Quantitative Tuberculin Test.—The author has attempted to determine the value of an intracutaneous test with properly diluted tuberculin, on the assumption that it is easily possible to determine a dilution of Old Tuberculin which will give a minimum of positive reactions of a certain size in patients who are clinically nontuberculous, and a maximum of such positive reactions in patients with active tuberculosis. It is assumed that 90 per cent of healthy adults will react positively to the ordinary tuberculin skin test (Pirquet or intracutaneous). Different dilutions of a given tuberculin were intracutaneously injected in a group of clinically nontuberculous ward patients. This tuberculin was carefully made up each week in dilutions of 1:1,000 to 1:10,000,000. Next the reaction of patients with active tuberculosis to these dilutions of tuberculin was determined. These were adult unselected patients with pulmonary tuberculosis in the wards of the Boston Sanatorium. Many were seriously ill, and some were moribund. Ninety per cent had positive sputum. A 1:50,000 dilution of Old Tuberculin injected into 202 nontuberculous patients was found to give 97 per cent negative results; that is, reactions less than 10 by 9 mm. in size. The same dilution injected into 82 patients with active tuberculosis gave 69 per cent of positive reactions, 10 by 9 mm. or more in size, and when severely ill patients with high fever and bronchopneumonic areas in the lungs were subtracted from the total tuberculous group, 93 per cent of the tuberculous patients gave adequate positive reactions 10 by 9 mm. or more in size. In seriously ill patients it is known that the allergic responses are diminished or absent, and their diagnosis is obvious without the dilute tuberculin test. With only 3 per cent of clinically nontuberculous patients reacting to the 1:50,000 dilution with areas 10 by 9 mm. or more, and from 69 to 93 per cent of such positive reactions in patients with active tuberculosis, such a test has apparently definite diagnostic value. No single focal or general reaction after the 1:50,000 dilution were encountered.—*The Intracutaneous Quantitative Tuberculin Test in the Diagnosis of Active Tuberculosis, D. Ayman, Jour. Am. Med. Ass., July 21, 1934, ciii, 154.*—(*G. L. L.*)

Specific Antibodies in Tuberculosis.—The sera of 105 individuals were used to demonstrate the presence of antibodies specific for tuberculosis. The new flocculation technique of Meinicke was employed. Sera from tuberculous and nontuberculous patients, from children inoculated with *BCG* and healthy individuals were tested. The results were divided into two series, A and B, and tabulated. Series A contained those cases which showed the characteristic single-tube reaction of Meinicke and at the same time a positive reaction for syphilis in the control tube. Series B was composed of those cases which gave negative reactions for syphilis and different types of Meinicke reactions in different tubes. Certain differences were noted in the comparison of the two series. In group B the number of positive reactions in healthy individuals is greatly reduced. In this same series, the scarcity of strongly positive reactions in the groups of patients without activity, in resolved and healed states, is an indication in favor of the greater specificity of the reactions. If further studies confirm the presence of specific antibodies in tuberculosis and if coexistent syphilitic antibodies can be eliminated then the Meinicke reaction will have better support. In cases showing tubercle bacilli in the sputum the positive results were 86.81 per cent in both series A and B. In doubtful cases, in cases without activity, in regressive and healing processes and in nontuberculous individuals negative or weak positive reactions were obtained in both series. Children vaccinated with *BCG* showed a greater number of positive than negative reactions but at the same time seemed to show, along with healthy individuals, no allergic state. Some subjects showed positive Meinicke reactions with negative tuberculin reactions while the reverse was true in other cases. Divergence between a positive allergic and a positive Meinicke reaction tends to show that the Meinicke reaction is not a test of activity but a test for the presence of antibodies in the blood stream. No conclusions can be drawn since the number of observations was so limited.—*Essai de diagnostic de la tuberculose par la réaction de Meinicke, P. Domingo &*

L. Sayé, Compt. Rend. Soc. Biol., November 10, 1934, cxvii, 595.—(M. T. W.)

Response to Antigens of Tubercle Bacilli.—It has been shown that colony variation in the acid-fast group of bacteria, in common with that of other species, is accompanied by variation in antigenic content. The experimental procedure consisted in determining the amount of complement fixed by sera in the presence of, first, an S antigen prepared from S organisms, and, second, in the presence of an R antigen by the quantitative complement-fixation technique of Wadsworth, Maltaner and Maltaner. As a further simplification, the specific fixation with the S antigen was divided by the specific fixation of the R antigen and the value called the S/R antibody index. In the present study this procedure has been followed, but the problem has been extended to include the rate of response of animals to repeated injections of heat-killed S and R organisms and to infection with tubercle bacilli. This was undertaken in the hope of formulating an explanation of complement-fixation results observed in cases of tuberculosis in man. When the serum from human subjects of pulmonary tuberculosis was subjected to antibody analysis by this method the cases fell into three categories; (a) cases with a high antibody index, 1.70 or higher, which resembles the reaction of rabbits subjected to long treatment with heat-killed S organisms which were for the most part acute progressive cases and on clinical grounds were given a poor prognosis; (b) cases with an intermediate antibody index, which proved to be about equally divided between those given, on clinical grounds, a good and an unfavorable prognosis; and (c) cases with a low antibody index, 1.25 or less, which resembles the reaction of rabbits subjected to long treatment with R organisms. These proved to be very largely chronic or healing cases. The results in rabbits subjected to a long course of immunization with heat-killed S tubercle bacilli show the development of antibodies which fix almost twice as much complement with S as with R antigens or the S/R antibody index approaches 2. Animals given a similar course of immunization with heat-killed R organisms develop antibodies which fix approximately the same amount of complement with S and R antigens or the S/R antibody index is only slightly over 1. In the course of immunization the response to heat-killed S and to heat-killed R organisms was initially the same, that is the S/R index remained low. But, as immunization with S organisms was continued beyond 4 to 6 doses, S specific antibodies increased to a much greater degree than the group antibodies, the S/R index increased. Similarly continued immunization with R organisms resulted in no change in the S/R antibody index. Two and one-half months after immunization was discontinued the specific S antibodies were found to be decreased in the sera of the animals to a greater degree than had the group antibodies. As a result, the S/R index had decreased. Infection of rabbits with S organisms caused a gradual increase in the S/R index, comparable with the response to heat-killed S organisms, followed by a decrease in both total antibody titre with S extracts and in S/R index as the S infection became generalized. Shortly before death, the reactivity with S antigens and the S/R index had fallen to approximately that of an untreated animal. Optimum proportion studies indicated the possibility of a small error in these measurements because of excess of antigen. It is concluded that tubercle bacilli, both S and R forms, contain a species of group antigen to which rabbits are relatively sensitive or responsive, and that S forms contain, in addition, an S-specific antigen to which rabbits show measurable response, as indicated by complement-fixation, ordinarily only after prolonged immunization.—*Rate of Response of Rabbits to Two Antigens of Tubercle Bacilli, G. B. Reed, C. E. Rice & B. G. Gardiner, J. Immunol., November, 1934, xxvii, 487.—(F. G. P.)*

Tuberculin Sensitiveness in Primary Tuberculosis.—Observations on the degree of tuberculin sensitiveness were made on 188 school children between 8 and 17½ years of age. Each child selected for study was sensitive to tuberculin, and the group was known to include 6 children with parenchymal infiltrations that later resolved, 132 children with characteristic calcified hilum lymph nodes or Ghon tubercles or both, twenty-one with negative chest plates, twenty-one with questionable calcifications in hilum nodes, and 8 children with pleural thickenings. The data recorded were based on a total of 1,864 surface-area determinations made on 466 Mantoux reactions to 0.1 mgm. of Old Tuberculin. In compiling the data for the 188 cases studied, averages were computed for 5 groups of children classified separately according to their roentgen examinations. The maximum size found for the reaction when measurements were taken at the end of four successive intervals of twenty-four hours each was accepted as indicative of the degree of skin sensitiveness. The average degree of sensitiveness to Old Tuberculin in the group of infected children with negative or inconclu-

sive chest films was found to be essentially equal to that present in groups of cases with demonstrable intrathoracic lesions considered characteristic of tuberculosis of first infection. The mean level of allergy to tuberculoprotein produced in groups of children by chance infections is independent, therefore, of the absence, presence, scarcity, abundance, size or character of the primary tuberculous lesions demonstrable by roentgen examinations during life. The distribution of different degrees of skin sensitiveness was also found not to differ essentially in the different groups. This study on living patients failed, therefore, to disclose evidence that justifies suspicion that children with large and intense intracutaneous reactions harbor more extensive pathological changes or have more active primary tuberculous lesions than do other children who are less sensitive to tuberculin. Apparently soon after tubercle bacilli make their initial entry into the body and before the primary tuberculous lesions have time to resolve, allergy reaches an average group level that is sustained with little or no change throughout the first few years that postdate the primary infection.—*Skin Sensitiveness to Tuberculin in Primary Tuberculosis: Is Its Degree in Children Related to the Extent of Demonstrable Intrathoracic Pathologic Changes Present?, C. A. Stewart, Jour. Am. Med. Ass., July 21, 1934, ciii, 176.*—(*G. L. L.*)

Tuberculin Allergy.—An allergic response is not the direct effect of the allergin on the tissue but rather the reaction of the tissue to the disturbance caused by the allergin in the equilibrium of the factors normally present in the tissue. This sensitivity of tissue equilibrium may be regarded as *Susceptibility* (S) as distinguished from *Reactivity* (R). These two characteristics are not constant in their relationship, although one may influence the other. They may vary in different degrees in different tissues, and in the same tissue, for example, the skin, at varying times. If the relative values of R and S are plotted, the line early in the course of a tuberculous infection would be straight. Later, depending on the course of the infection, the line may deviate in one direction, in favorable cases, toward a state of *diaphory* or, in cases that become rapidly worse (haematogenous dissemination) toward a state of *anergy*. In both instances the tuberculin reaction itself is very weak; in the former because of low susceptibility, in the latter because of low reactivity. In the chronic case of tuberculosis with relapses from time to time, the curve of coördination between S and R would be zig-zag. This conception is not only of value in considering the prognosis in a case of tuberculosis but is in accord with the rationale of seeking a modification of tuberculin extract for therapeutic purposes which will decrease its toxicity without impairing the power of bolstering the reactivity of the tissues.—*Tuberkulose-studien. I. Tuberkulose in Ordinatensystem der Allergie, F. v. Gröer, Ztschr. f. Kinderhk., July, 1934, lvi, 379.*—(*M. D.*)

Tuberculin Allergy.—This study was carried out in order to confirm experimentally the existence of the two factors, Susceptibility (S) and Reactivity (R) of tissue in exhibiting an allergic response. Since neither of these factors can be varied at will, observations were made of the variation in the size of the tuberculin reaction with variation in the concentration of the tuberculin extract. Three possible types of variation may be expected in this type of study: (1) In individuals with S and R relatively the same, there should be a fairly constant relationship between tuberculin concentration and intensity of reaction; (2) with relatively high S and low R, reactions to low concentrations would be almost as intense as to large; and (3) with relatively low S and high R, reactions to high concentrations would be relatively (as well as absolutely) more intense than to low.

Actually, the children studied could be grouped into these 3 types by measuring the size of the reactions to varying concentrations of tuberculin from 1/100 to 1/1,000,000 (0.1 cc. intracutaneously). In the first group the product of the size of the reaction (millimetres) and the negative log of the concentration was practically constant irrespective of the concentration. In the second group the product increased as the concentration diminished; that is, the reactions, although somewhat smaller with decreasing concentration, were relatively not as much smaller as would be expected if the product were constant. In the third group the reactions to the lower concentrations were much smaller than expected if the product were constant. The type of allergy exhibited in the first group is *homodynamic*, in the other groups *heterodynamic:* either (1) *pleoaesthetic* (S>R) or (2) *pleoergic* (R<S).—*Tuberkulosestudien. II. Über die Abhängigkeit der Ausdehnung intracutaner Tuberkulinreaction von der Tuberkulinkonzentration und die dynamische Differenzierung der Tuberkulinallergie im Kindesalter: die homodyname und heterodyname Allergielage, Fr. v. Gröer & A. v. Chwalibogowski, Ztschr. f. Kinderhk., July, 1934, lvi, 390.*—(*M. D.*)

Prolonged Allergy to Dead Tubercle Bacilli.—Tubercle bacilli are autoclaved

and added to boiling paraffin with a melting point of 42° to 54°C. After cooling, the mixture is injected subcutaneously, where it solidifies. At the end of a month tuberculin sensitiveness can be elicited in both rabbits and guinea pigs. The allergy persists for more than a year. Contrary to the general belief that paraffin acts entirely as a foreign body, and without any possibility of exchange between it and the tissues, the author states that a Koch phenomenon can be elicited in a tuberculous animal by the introduction of living tubercle bacilli incorporated in melted paraffin. The paraffin is broken up by the invading tissues into islands and surrounded by epithelioid and giant cells. No caseation develops at the site of injection of paraffin alone. If dead tubercle bacilli are added to the paraffin prominent caseous foci appear in the paraffin focus. At the end of six months the focus is converted into a well-encapsulated caseous abscess.—*État allergique durable, obtenu chez les animaux de laboratoire par injection sous-cutanée de bacille tuberculeux morts enrobés dans la paraffine solide, E. Couland, Rev. Tuberc., October, 1934, ii, 850.*—(*M. B. L.*)

Sensitization of Guinea Pigs to Killed Tubercle Bacilli.—The material for this study was provided by 58 guinea pigs which survived one year after injection of one dose of tubercle bacilli exposed to weak concentrations of phenol, formalin and merthiolate. These animals showed no evidence suggesting tuberculous infection, and survived a large dose of Old Tuberculin intraperitoneally, and necropsies a year after injection showed no signs of tuberculosis. It was, therefore, concluded that they were free from living tubercle bacilli. On the fifty-ninth day of the experiment referred to (when the animals were injected with chemically treated bacilli) each guinea pig was given 0.2 cc. of a 1 per cent dilution of Old Tuberculin (International Standard), and the reactions were measured, described and recorded eighteen and forty-eight hours after. Nearly all gave positive skin reactions. Animals obviously infected, showing enlarged lymph nodes and later generalized tuberculosis at necropsy, were not included in this later study. But 51 of 58 animals surviving for a year without evidence of tuberculous infection during life or at necropsy showed with standard Old Tuberculin definite skin reactions in many ways similar to that presented by tuberculous guinea pigs. At first it was thought that these animals really were infected and that evidence of this would eventually manifest itself. At the end of a year, however, with no such evidence demonstrable, the view is now held that these animals had been sensitized to Old Tuberculin by a single small dose of tubercle bacilli chemically killed by relatively weak dilutions of antiseptics acting over varying periods. *Characteristics of "sensitization" reactions:* Generally these appeared the day following the tuberculin test, usually as a rounded regular erythematous area, 15 to 20 mm. or larger in diameter, nearly always slightly oedematous. After forty-eight hours they diminished and by the third day had disappeared. In summary, 88 per cent of the 58 animals gave such definite reactions thirty-two to fifty-nine days after injection, and in two-thirds of these the hypersensitive state persisted over a year, though the later reactions were smaller and less intense. *Discussion and interpretation:* That guinea pigs can be sensitized to Old Tuberculin by the injection of dead tubercle bacilli is well known. Heat-killed bacilli were most used by earlier investigators, but some investigators have used carbol-fuchsin or ether. In general the present study confirms the conclusions of Bohart and Tytler. The sensitizing constituent of the bacillus, probably protein, is apparently not appreciably damaged by chemical treatment such as described. A comparison was undertaken with the sensitizing effects of various "tubercle vaccines," but seventy-six days after their administration, reactions to intracutaneous injection of 2 mgm. of Old Tuberculin were completely negative except in those animals previously inoculated with *one* of the 10 vaccine preparations mentioned. In these animals the intracutaneous tuberculin reactions were definite and marked. *Comparison of effects on sensitized guinea pigs of various tuberculin derivatives:* At intervals varying from 277 to 304 days after injection of the killed tubercle bacilli, the 58 guinea pigs referred to received simultaneous intracutaneous injections of 2 mgm. (0.2 cc. of 1 per cent solution) of 7 substances prepared from Old Tuberculin or Bouillon Filtrate, together with the same quantity of International Standard Old Tuberculin. It was already known that four of the substances were of equal or greater tuberculin potency (tested on tuberculous guinea pigs) than the standard, and two less. The other was the carbohydrate derivative. *Results: 1:* None of the 58 animals reacted to the carbohydrate intracutaneously. *2:* Fifteen failed to react to Standard Old Tuberculin or to any other derivative. *3:* Seventeen gave marked reactions to all substances except the carbohydrate. *4:* Seven animals reacted to the standard tuberculin and three other substances. *5:* Nineteen reacted to the above and to a lesser and variable degree to the other substances. Thus, guinea pigs sensi-

tized by killed bacilli seem to react more constantly to Standard Old Tuberculin than to any of its derivatives. It is thought that these observations support Petroff and Stewart's view that skin hypersentiveness produced by killed bacilli is similar but more uniform than that produced by infection.—*The Sensitization of Guinea Pigs Following a Single Injection of a Small Dose of Dead Tubercle Bacilli, S. R. Douglas & P. Hartley, Tubercle, December, 1934, xvi, 100.*—(*A. P.*)

Spectral Analysis of Purified Tuberculin.—By use of the ultraspectrographical method, a substance showing selective adsorption with a maximum at 267 mμ, was found to be present in all tuberculin fractions, made from human, bovine and avian types of tubercle bacilli which had been purified by means of trichloracetic-acid precipitation, and even in amounts corresponding to the potency of these fractions. The small amount of this substance present could be removed by means of ammonium-sulphate precipitation, with no loss in tuberculin potency, and therefore it cannot be considered essential in eliciting the tuberculin reaction. This substance was identified as thymus nucleic acid, by means of analysis for phosphorus and comparative spectrographical examination. It was not found to be present in fractions made from the nonpathogenic acid-fast bacilli, timothy, butyricum and smegma. Irradiation with ultraviolet rays, which diminished or destroyed the potency of tuberculin fractions, had a corresponding effect on the selective absorption.—*Spectral Analysis of Purified Tuberculin, Mona Spiegel-Adolf and Florence B. Seibert, J. Biol. Chem., August, 1934, cvi, 373.*—*F.B.S.*

Precipitins for Fractions of S and R Tubercle Bacilli.—Titration of sera from human cases of tuberculosis with whole S and R tubercle bacilli extracts have revealed differences bearing some relation to the activity of the tuberculous infection. The present study represents a preliminary search for the general chemical fractions possessing the most S- specific and species-specific antigenicity. The *lipoid*, *protein* and *carbohydrate* fractions were obtained from S and R tubercle bacilli respectively. These fractions were not entirely purified; hence they are crude chemical extracts. The antisera were prepared by repeatedly injecting rabbits (intraperitoneally) with heat-killed cultures, one group with S, another with R, and a third group with mixed S and R vaccines. Eighteen antisera were tested with the 6 crude chemical preparations for precipitin activity. Also the precipitin titers of S and R antisera with purified albumen, globulin and polysaccharide from an undifferentiated culture of virulent human tubercle bacilli were determined. The protein, lipoid and carbohydrate fractions prepared from S or R tubercle bacilli all showed precipitin reactions with sera of rabbits immunized with either S or R whole bacilli. None of the chemical fractions was specific for one variant type only, although the protein fractions, and possibly the carbohydrate, exhibited a certain degree of specificity. Unless all fractions were contaminated with common substances, there appeared to be similar protein, lipoid and carbohydrate in both variant forms. Differences of the magnitude previously shown by complement fixation were not indicated by the precipitin titration. Lipoid fractions showed no type specificity. During the process of immunization with killed S tubercle bacilli, there is a relative increase in precipitins for proteins and carbohydrates from S organisms over that of precipitins from R proteins and carbohydrates. R antisera, on the other hand, increased in relative reactivity with R protein. S antisera reacted relatively more strongly with purified globulin and polysaccharide preparations made from virulent cultures of human tubercle bacilli than did R antisera. The latter gave a relatively stronger reaction with purified albumen.—*Development of Precipitins for Protein, Lipoid and Carbohydrate Fractions of S and R Forms of Tubercle Bacilli, C. E. Rice, J. Immunol., January, 1935, xxviii, 19.*—(*J. S. W.*)

Culture Medium for Tubercle Bacilli.—By using Loewenstein's medium, as modified by K. A. Jensen at the State Serum Institute of Copenhagen, it has been possible to discover the presence of tubercle bacilli in material otherwise reported as negative, in a high percentage of cases. Sputum and pleural fluids became positive in about 17 days. The typing of bacilli, easily done for growth of either human or bovine type, is characteristic. If no growth appears on the medium in four weeks it may be reported negative, but the tubes should be incubated another 3 or 4 weeks because growth may occur. This is especially true of the bovine bacillus. The medium should be carefully prepared and screw-top bottles are preferred to tubes for this medium. Mineral-salt solution contains 0.4 per cent potassium sulphate, 0.4 per cent magnesium sulphate, 0.1 per cent magnesium citrate, and 0.6 per cent asparagin, 2.0 per cent glycerine, and distilled water, which should be heated over a gas-ring to dissolve. When

dissolved, the material is boiled or placed in an open autoclave at 100°C. for 2 hours and allow to cool at room temperature over night. To every 600 cc. of the above solution, 30 gm. of potato flour is added, over a water-bath and stirred constantly for 15 to 20 minutes; and then allowed to stand one hour at 56 degrees. Hen's eggs, less than a week old, are washed in 5 per cent soft soap solution and left in running water from one to two hours. They are broken under sterile conditions into a sterile container, and the yolks and whites thoroughly homogenized by stirring or shaking in a mechanical mixer. At the end of the hour in the water-bath, the salt-potato solution is added to the egg-fluid in the proportions of 600 cc. of solution to 1 litre of egg-fluid. To each 1600 cc. of this mixture, 20 cc. of 2 per cent malachite-green is added after it has been incubated from 1 to 2 hours. The medium should be tubed and slanted before it cools. The tubes are heated in an oven or inspissator to 85°C. for half an hour and again heated to 75° for half an hour the following day. Test-tubes should be stored in the cold, but the screw-topped bottles will keep indefinitely at any temperature.—*The Value of Culture in the Solution of Problems of Tuberculosis, E. M. Holmes, J. State Med., October, 1934, xlii, 559.*—(*L. F. B.*)

Free Growth Period of Tubercle Bacilli.—A useful approach to the problem of immunity in tuberculosis is the attempt to discover how the tubercle bacillus itself, with its resistant waxy structure, is affected by inoculation in the normal and the "immune" animal. The use of omental spreads makes it possible to study the inoculated bacilli in their normal relation to the fixed tissue cells and the developing tubercles, a study that cannot be made adequately either with histological sections or with smears of the body fluids. Young guinea pigs were used in the experiments, as the omenta of old guinea pigs contain too much perivascular fat to make good spread preparations. In most of the experiments H37 human tubercle bacilli were used as the inoculum. In general the animals were given a suspension containing 0.1 mgm. of bacilli per 100 gm. of body weight, the injection being made intraperitoneally. Great care was taken to avoid penetrating the bowel. In order to follow the rapid omental changes animals were killed at daily intervals or more frequently. That part of the omentum which showed maximum involvement was freed with scissors and mounted on a clean glass slide, either directly or after first floating the tissue in physiological salt solution. With minor exceptions the ordinary Ziehl-Nielsen technique for staining was employed. Decolorization (3 per cent HCl in 95 per cent alcohol) was somewhat prolonged (10 minutes) in an attempt to decolorize the thicker portions of the preparation. The process was completed by immersing the thoroughly dried preparation in absolute alcohol, then in xylol, and mounting in balsam. In the normal guinea pig the bacilli were found to be first taken up by the polymorphonuclear cells. The large clumps of bacilli present in the inoculum disappeared rapidly, being almost completely broken up by the polymorphonuclears. At two hours there were relatively few large mononuclear leucocytes; in no case were these cells phagocytosing the polymorphonuclears. After twenty-four hours many of the polymorphonuclears which had phagocytosed bacilli were engulfed by the large mononuclear cells, the bacilli thus undergoing a double phagocytosis. Occasional mononuclear cells were seen to take up bacilli directly. Also, polymorphonuclears bearing tubercle bacilli now apparently have gravitated to the milk spots of the omentum or to the perivascular fat tissue. Within 3 days after inoculation the perivascular areas became dense cellular masses composed largely of mononuclear cells believed to be derived from the omentum itself. At 4 days the preparations showed a hitherto unreported phenomenon. In association with the omental cells, masses of bacilli were seen growing in parallel strands just as they might grow on the surface of glycerine-broth. These bacilli grew adjacent to or looped around the cells and showed no sign whatever of attracting cells of the inflammatory type. These organisms, because of their capacity for growth without the least interference from either the cells or body fluids of the animal in which they are proliferating, have been termed *freely growing bacilli*. These organisms did not represent clumps of bacilli from the inoculum. These clumps had already disappeared. From the fourth day the number of animals showing the freely growing bacilli rose at six days to 81 per cent and 89 per cent at 7 days, but fell off abruptly after the seventh day. A series of animals were inoculated with caseous material obtained from cold abscesses. Smears of the inoculum showed only rare acid-fast bacilli. In every series, however, masses of freely growing tubercle bacilli made their appearance. The results from the inoculation of hypersensitive pigs contrasted strongly with the above. The clumps of bacilli which were included in the inoculum were not broken up by phagocytosis. These clumps were seen to be closely surrounded by polymorphonuclear leuco-

cytes but were only rarely phagocyted. Furthermore, at no time in the hypersensitive animals was the phenomenon of free growth of the inoculated tubercle bacilli observed. Since normal rabbits are highly resistant to the human type of tubercle bacilli, it was decided to inoculate some of these animals. None of the rabbits showed at any time any free growth of tubercle bacilli. As mentioned above, the free growing bacilli rapidly disappeared after the seventh day when they again attracted the polymorphonuclear cells, and by 9 days there was definite evidence of the formation of a secondary series of tubercles. It is not definitely known whether the abrupt reappearance of positive chemotaxis and the concomitant disappearance of the freely growing bacilli are due to the development of immune bodies in the infected animal or to changes in the bacillus itself, or to both. Free growth does not occur in a tuberculin-sensitive animal. Since freely growing bacilli disappear *before* the tuberculin test becomes positive, it may be that a more delicate test, if we had one, would indicate that the changed condition (allergy) had already begun to exist. The difference between the types of reaction elicited in the normal and immune animals would seem "qualitative" rather than "quantitative" in nature when viewed in the light of the different effect upon the growth of the tubercle bacillus during the first week after inoculation. Contrary to the general belief the polynuclear leucocyte plays an important rôle in the immune process of tuberculosis. While it is true that tubercle bacilli are disseminated by these leucocytes following a primary infection, it is also evident that the bacilli grow at a certain period in perfect symbiosis with the omental cells which are closely related to the clasmatocytes. It is, however, the polymorphonuclears that first attack and break up the freely growing bacilli and initiate the process of renewed tubercle-formation. They, also, in hypersensitive guinea pigs are plastered about the clumps of inoculated bacilli—not phagocytosing them but preventing the clump from breaking up, helping to localize the bacilli and, possibly, helping to prevent the free growth of bacilli which occurs in the normal animal.—*A Free Growth Period of Tubercle Bacilli in the Guinea Pig Omentum as Related to the Hypersensitive State, C. E. Woodruff, Am. J. Path., November, 1934, x, 739.—(J. S. W.)*

Staining Variability of the Tubercle Bacillus.—By the Giemsa stain 2 types of tubercle bacilli were distinguished in tuberculous foci: (1) a basophilic form, usually slender, occurring in epithelioid cells, caseous tissue and regions of recent liquefaction, and (2) an eosinophilic form, usually plump and granular, occurring, commonly in large numbers, in old caseous and calcified foci or foci of recent exacerbation. The eosinophilic property was believed associated with a state of inactivity or one of increased resistance of the bacilli. The eosinophilic form corresponded partially to non-acid-fast forms, whether the latter represented the early stage of growth or a stage of degeneration. Histological sections of cultures demonstrated 4 forms of bacilli: (1) non-acid-fast granules, (2) ordinary acid-fast bacilli not staining with Mallory's stain (chromophobic bacilli), (3) super-acid-fast bacilli, staining intensely with Mallory's stain (chromophilic bacilli), and (4) "zoogloea" (chromophilic substance). Rapidly growing cultures, from the sputum or urine of patients with large cavities, contained chiefly chromophilic bacilli or chromophilic substance. The amount of chromophilic substance depended on the rapidity of culture growth and was not related to the virulence of the microörganisms. Chromophilic bacilli, however, on intracutaneous injection, caused larger and more rapid infiltrations in both normal and allergic guinea pigs, than did cultures without the chromophilic substance.—*Histological Studies on the Variability of the Tubercle Bacillus, W. Pagel, J. Path. & Bact., November, 1934, xxxix, 689.—(E. R. L.)*

Types of Tubercle Bacilli Isolated from Man.—From patients with tuberculosis 2,500 strains of tubercle bacilli were isolated and typed. They were cultivated on asparagin-egg medium with and without 0.75 per cent glycerine. Most of the strains were identified as either human or bovine, and only a few exhibited deviations from the main types. These showed the dysgonic type of growth, resembling the bovine-type bacillus. The fact that they were highly virulent for guinea pigs and had low pathogenicity for rabbits indicated they were human-type bacilli. These dysgonic human-type strains may dissociate into dysgonic and into eugonic forms showing vigorous growth on glycerinated medium, but the reverse mutation never occurs. The virulence of the two forms is the same, contrary to Petroff's findings with the R and S forms. One bovine strain, out of 300, was of dysgonic form and dissociated into a dysgonic and into a eugonic form which was pigmented. These two forms were equal in virulence for guinea pigs and rabbits. The dissociation is assumed to be caused by a varying ability of the tubercle bacilli to

adapt their growth to glycerine.—*Studies on the Types of Tubercle Bacilli Isolated from Man, I. K. A. Jensen & J. Frimodt-Möller, Acta Tuberc. Scandinav., Fasc. 3, 1934, viii, 153.*—(*F. B. S.*)

Acid-Fast Bacillus Simulating Avian and Human Strains.—An acid-fast bacillus designated as *Bacillus C* was isolated from a guinea pig inoculated with spinal fluid of a child with a nervous syndrome. This bacillus possessed atypical staining and cultural properties. On egg medium it produced creamy, yellowish-white, smooth colonies. Cultures, concentrated as for tuberculin, produced, in doses of 0.1 cc. of a dilution of 1 to 1,000, positive skin reactions in tuberculous guinea pigs and in guinea pigs infected with the *Bacillus C*, but without toxic reactions. The animals tolerated as much as 1.5 cc. without showing anything more than a passing malaise and a large scab at the site of inoculation. The *Bacillus C* is only slightly pathogenic for the guinea pig. Subcutaneous inoculations of 1 to 10 mgm. produced only local abscesses, which persisted sometimes as long as five months, with slight hypertrophy of the corresponding lymph nodes. The liver, spleen and lungs appeared normal, but yielded the *Bacillus C* in pure culture. The infected animals reacted to tuberculin (0.1 cc. of dilution of 1 to 10) during the course of the second week. At the end of the second month the skin reaction became necrotic. The intracutaneous inoculation of 0.1 mgm. produced a small red nodule which ulcerated about the fifteenth day and then slowly regressed. No visceral lesions developed. Following intraperitoneal inoculations of 2 mgm., purulent nodules developed in the omentum. The rabbit tolerated without apparent damage 10 and even 20 mgm. of the *Bacillus C* inoculated intravenously. No visceral lesions were found, save a slight enlargement of the spleen in animals killed six to ten weeks after inoculation. Chickens, inoculated intravenously with 2 mgm. and killed ten weeks later, remained grossly normal, but cultures of the spleen were positive. Mice died in from ten to fifteen days after intraperitoneal inoculations of 10 mgm., with the omentum dotted with nodules and the spleen enlarged. *Bacillus C* has some properties of human and avian tubercle bacilli. It differs from the paratubercle bacillus by the fact that it gives to the guinea pig an accentuated allergy. Tuberculin produced from it equalled one-half of the Koch's bacillus tuberculin when measured by the skin reaction.—*Caractères d'un bacille acido-résistant isolé d'un cobaye inoculé avec un liquide pathologique d'origine humaine, P. Boquet, Compt. Rend. Soc. Biol., November 17, 1934, cxvii, 659.*—(*M. T. W.*)

Atypical Acid-Fast Bacillus.—A two-and-one-half-year-old child, living in contact with a tuberculous father but in apparent good health, suddenly developed convulsions. A lumbar puncture was made, but no acid-fast organisms were found in the spinal fluid on microscopical examination. Cultures were made and 2 guinea pigs inoculated. These cultures remained sterile after an indefinite period of incubation. The tuberculin reaction in the guinea pigs on the twelfth day after inoculation was negative but became positive in six weeks. There was no evidence of abscess at the site of inoculation and the corresponding lymph nodes were only slightly enlarged. At the end of three months the allergic reaction was slightly increased, and a large, reddened papular thickening, necrotic only in the centre, had developed. One guinea pig was killed at the end of four months. Its organs, grossly free from any tuberculous lesions, were cultured and inoculated into 2 guinea pigs. The second guinea pig of the first series which still showed a positive tuberculin reaction at the end of the fourth month was killed. No tuberculous lesions could be found at autopsy. The liver, spleen, inguinal and sacral lymph nodes were cultured. Three weeks later small, round grayish colonies of acid-fast bacilli appeared in the culture-tubes inoculated with the lymph nodes. Guinea pigs inoculated with tissues from the first guinea pig became sensitive to tuberculin in six weeks. One was killed. Cultures of the lymph nodes again yielded acid-fast bacilli. This acid-fast organism is not compatible with a paratubercle bacillus, which is sometime capable of transmitting allergy to the guinea pig and producing paratuberculous lesions. Elsewhere it has been shown that saprophytic paratubercle bacilli inoculated in the suboccipital region are harmless for rabbits. The *Bacillus C* inoculated in the same way produces paralysis and death. A very small dose of variant S of both human and bovine strains of tubercle bacilli also produce fatal meningitis. There is also a difference between the haptenes and antigenic properties of the paratubercle bacilli and the *Bacillus C* and this atypical acid-fast bacillus. In view of the fact that the cultures made directly from the spinal fluid of the child were sterile the question arises whether the acid-fast bacillus that was recovered came from the spinal fluid or whether the guinea pig was already infected at the time of inoculation. It has been shown in the same laboratory that guinea pigs in apparent good health do some-

times harbor acid-fast bacilli, some of which are capable of producing a lasting allergy. Nevertheless the uncertainty surrounding the source of this bacillus remains. It appears to be more like the tubercle bacillus than the paratubercle bacillus.—*Remarques à propos d'un bacillie acido-résistant, A. Boquet, Compt. Rend. Soc. Biol., November 17, 1934, cxvii, 662.—(M. T. W.)*

Non-acid-fast Tubercle Bacilli.—Various authors, including Møllgaard himself, have published findings concerning non-acid-fast tubercle bacilli. In this last study Møllgaard reaches the conclusion that all these microörganisms are not tubercle bacilli and are not, as frequently supposed, developmental forms of tubercle bacilli. Møllgaard isolated, frequently from tuberculous tissues, white actinomyces and he believed, for some time, that they were a part of the life-cycle of tubercle bacilli. Now it is stated that they represent a totally different microorganism, which, however, is frequently found in symbiosis with tubercle bacilli, both in tissues, and in so-called pure cultures of tubercle bacilli. These actinomyces are pathogenic. They occur in the form of diphtheroids and streptoconidia. The slightly virulent cultures of the vegetative diphtheroid forms produce, in guinea pigs, lymphadenitis, particularly of the bronchial lymph nodes, serositides and cachexia, and, at times, tubercular foci in lungs and spleen. Freshly isolated cultures cause, on intravenous injection, a clinical picture, which is very similar to acute rheumatic fever and polyarthritis, which is characterized by serous pericarditis, verrucous endocarditis and polyarthritis. In addition there occur pleuritides and serous meningitis. Around the infected joints, cold abscesses may develop. The streptoconidia cause hilar lymphadenitis and tubercular lesions in lungs, liver and spleen. In tuberculous tissues, there must occur therefore, very frequently, two different pathogenic microorganisms: the tubercle bacillus and the non-acid-fast *Actinomyces alba*. In tuberculous patients, more than 90 per cent show a positive skin reaction with nonprotein toxin isolated from the actinomyces. It is concluded that a pure infection with tubercle bacilli produces chronic productive pulmonary tuberculosis and tuberculous granulomata in various organs. Pure infection with *Actinomyces alba* produces lymphadenitis, serositis and endocarditis, in other words a disease similar to, or identical with, acute rheumatic fever. An infection caused by both organisms produces a mixture of specific tuberculous granulation tissue with serositides and caseous pneumonia, Perlsucht-like caseating lymph nodes and cold abscesses. All the pathogenic action that is ascribed by Calmette and his coworkers to the filterable form of the tubercle bacillus is believed to be due to the actinomyces, and it is assumed that the actinomyces infection prepares the ground for genuine tuberculosis.—*Untersuchungen über die biologischen Eigenschaften und die pathogene Wirkung der sogenannten nicht säurefesten Tuberkelbacillen, H. Møllgaard, Beitr. Klin. Tuberk., December, 1934, lxxxv, 616.—(M. P.)*

Dissociation of Human Tubercle Bacilli.—In experimental tuberculosis in animals the lack of uniformity of infection and the variability in the extent of the disease have long been noted. Two main factors have been offered in explaining this irregularity; namely, the natural resistance of the host and the virulence of the organism. Considering the latter factor only, why should an apparently virulent culture show variations in infectiousness? Accepting the hypothesis that in any culture not every member possesses the same degree of virulence for experimental animals, it follows that the virulence of the culture will depend largely on the ratio of the virulent to the nonvirulent (or low virulent) members of the culture. By assorting and eliminating we should be able, eventually, not only to separate the two types, but also to stabilize their virulent and nonvirulent characteristics by cultivating them in suitable environments. The present studies deal mainly with the dissociation of the human tubercle bacillus into two variants, one virulent and the other avirulent. The method was as follows: *1:* Cultivating the organism for a considerable period on glycerol-potato-bile medium (Calmette), a medium which has been successfully used for diminishing virulence. *2:* Subsequent cultivation for assortment and elimination (single-colony study), and, especially where the R avirulent variant was desired, cultivation on solid and fluid medium of pH 6.1. A human tubercle bacillus H37, which for the last 29 years has been extensively employed in experimental tuberculosis and for the preparation of tuberculin, was used in this study. The two variants obtained, R (rough, avirulent) and S (smooth, virulent), have a colony morphology which is typical and distinctive for each on repeated cultures. Both are gram-positive and acid-fast. The S are short solid rods, sometimes slightly curved, varying in length from 2 to 5 micra. Beaded forms may be present but granules are absent. The R bacilli are pleomorphic and larger in size. Some are club-shaped; others straight, filamentous, long, beaded rods; and

still others appear in branching forms. Granules are present in young cultures. The growth pH curve of both variants follows that observed for any undissociated human type of tubercle bacillus. From the variants tuberculins were prepared. Both tuberculins elicited the same type and intensity of reaction in guinea pigs sensitized with heat-killed R and S variants. The S variant was found highly virulent for guinea pigs whereas the R variant had little or no virulence. A further dissociation of the S variant was attempted, starting with a single definite colony. The same general procedure was followed as in the first experiment, and typical and atypical S colonies and a large number of crater-like R colonies were obtained. Subculture of the R and S variants on suitable media was continued until the two types were further stabilized, and at intervals animals were inoculated to test for virulence. There is a marked difference in virulence, as demonstrated by pathogenicity, between typical H37 R and S variants. The R variant had a low virulence and is very slightly pathogenic. It caused no mortality *per se*, very little gross evidence of tuberculosis, and a corresponding small number of microscopic lesions. These were small, usually nonprogressive, were composed chiefly of proliferation, very rarely contained caseation, and retrogressed early (the so called "hard" tubercle). On the other hand the S variant had a high virulence and pathogenicity. It produced large widespread lesions, with all the characteristics of the so called "soft tubercle." Variants of different dissociates, or from replants of the same dissociation, have slightly different levels of virulence. Blood studies were made on the variant groups of two series of guinea pigs and one series of rabbits. The avirulent variant (R) produced a retrogressive infection and blood-curves which reverted to normal. The virulent variant (S) produced a progressive, septic, allergic infection and the blood-curves indicate these conditions to a certain extent. Virulence is the *in vivo* manifestation of propagation and it depends on some as yet undefined constituent. Colony morphology is the *in vitro* manifestation of growth and it too depends on the bacillary constituents. The result of dissociation of a strain forces a reconsideration of the host-parasite relationship in which it may be involved. Its virulent variant may grow in a species which is not naturally favorable soil; the avirulent variant may fail in an ordinary susceptible species. The responsibility for virulence thus belongs increasingly to the bacillus and less to the host. It is quite possible that there will be a further change in virulence of the two variants following repeated cultivation. The present series of subcultures show an increasing differentiation. The decrease in virulence of the H37 R, when compared with the parent culture, is more notable than the increase in virulence of the S. This is probably due to the original relatively high virulence of the H37 strain. It is possible that other means of forcing a dissociation may be discovered.—*Biological Studies of the Tubercle Bacillus. III. Dissociation and Pathogenicity of the R and S Variants of the Human Tubercle Bacillus (H37), W. Steenken, Jr., W. H. Oatway, Jr., & S. A. Petroff, J. Exper. Med., October 1, 1934, lx, 515.*—(*J. S. W.*).

Biological Properties of Tubercle Bacilli Producing Smooth Colonies.—The biological properties of certain strains of tubercle bacilli isolated from tuberculous guinea pigs injected with an acetone extract of Koch's bacilli are presented. The smooth strains which developed from this procedure were not virulent for the guinea pig, but, on the other hand, sensitized it to tuberculin. They possessed a toxic factor for the rabbit and chicken at the moment of their isolation which they lost after reinoculation on culture medium. One smooth strain was pathogenic for the rabbit and chicken and nonpathogenic for the guinea pig. After its first reseeding on potato-glycerine medium, it produced typical R colonies and then became pathogenic for the guinea pig. Another strain lost its pathogenicity for the rabbit and chicken after several subcultures. Guinea pigs were vaccinated with a smooth strain which was toxic for the rabbit and chicken and with another which was marked by its absence of toxicity. These guinea pigs and control guinea pigs were inoculated with a virulent human strain of tubercle bacilli. At autopsy the vaccinated and control animals showed the same type of lymph-node involvement. The control guinea pigs showed a generalized infection while the others were free from organic involvement. It would seem that these smooth-colony-producing bacilli, by virtue of their initial toxic, immunizing and reversible powers belong in the group of tubercle bacilli but in a lower form.—*Sur certaines propriétés biologiques des cultures lisses de bacilles tuberculeux obtenus par la méthode des injections d'extrait acétonique de bacilles de Koch, L. Nègre & J. Bretley, Compt. Rend. Soc. Biol., January 26, 1935, cxvii, 295.*—(*M. T. W.*)

Dissociation of Dysgonic Type of Bovine Tubercle Bacilli.—Cultures made from the spleen of a guinea pig inoculated

with a tuberculous lymph node from a bovine source yielded small, grayish-white, smooth colonies, some of which became typical rough colonies. These R colonies all developed readily in subcultures and remained virulent for the guinea pig and rabbit. Another eugonic type was observed developing from the surface of a dysgonic form. Dysgonic types may dissociate into eugonic types on ordinary media but, with the aid of a specialized medium (Besredka's medium is recommended), this dissociation is facilitated. The virulence of the two types remains unchanged.—*Étude des caractères morphologiques et de la dissociation des bacilles tuberculeux bovins dysgoniques, R. Laporte & U. Battaglini, Compt. Rend. Soc. Biol., January 26, 1935, cxvii, 304.*—(*M. T. W.*)

Isolation of Tubercle Bacilli from Larynx.—The method of Blume (1906) who used smears from the larynx as a complementary method of the examination of the pulmonary sputum is warmly recommended. In the absence of sputum the smear from the larynx often makes possible the finding of bacilli. The culture media of Petragnani or Hohn and Loewenstein are used. A positive finding may be obtained within a period of twelve to twenty-eight days after inoculation. Of 236 patients who gave no other positive results, 95 showed a positive sputum obtained by the examination of the laryngeal smear. Only by this method it is permissible to make a definite statement that a patient's sputum has become negative.—*Die Kultur von Tuberkelbazillen aus Larynxabstrichen, J. Schramek & P. Hegedues, Klin. Wchnschr., February 16, 1935, xiv, 237.*—(*F. G. K.*).

Tubercle Bacilli in Omentum and Peritoneal Exudate of Guinea Pigs.—For the comparative study of the tenure of tubercle bacilli in primary infections and in reinfections of the peritoneum of guinea pigs, the exudate and omentum were cultured in measured amounts. At varying times after peritoneal inoculation a guinea pig primarily infected and one reinoculated were killed. The results were grouped into 4 series and tabulated, two for the results of the cultures of the peritoneal fluid and two for the omentum. The same strain of bovine tubercle bacilli was used through the entire experiment. *Series 1:* Six guinea pigs were inoculated with 0.001 mgm. of bacilli two to four months apart, four subcutaneously and two intratracheally. At the same time 6 new guinea pigs received intraperitoneal inoculations of 0.01 mgm. Peritoneal punctures were made from the second to the seventy-fifth days and cultured. *Series 2:* The guinea pigs infected intratracheally and 6 new ones were given, six weeks later, 0.001 mgm. of bacilli intraperitoneally. Cultures from peritoneal punctures were again made. From these two series of experiments it appeared that the tenure of cultivatable bacilli from the peritoneal fluid in the reinfected animals was weaker than in the controls. The exudate from the reinfected animals may be sterile or contain only a rare bacillus except in some instances as the animal approaches death. Series 3 and 4 comprised studies of the omentum. *Series 3:* Four reinoculated guinea pigs and 4 controls were killed twenty-four hours, and six, twelve and twenty days after intraperitoneal inoculations of 0.01 mgm. of tubercle bacilli. Cultures of the omentum, made twenty-four hours after inoculation, were sterile, while all the others were positive. All the cultures of the omentum of the primary infection yielded innumerable confluent colonies. With the reinfected guinea pigs the number of colonies was 260 on the sixth day, 326 on the twelfth day, and 380 on the twentieth. It should be noted that the dose in this series was elevated. *Series 4:* Six guinea pigs, infected with 0.001 mgm. of tubercle bacilli intratracheally, received two months later, at the same time as 3 controls, intraperitoneal injections of 0.001 mgm. of bacilli. A guinea pig of each series was killed at varying intervals from twenty-four hours to thirty-two days. In this series the difference is marked between the two types of infected animals, the tenure being greater in the primary infections. These experiments support the theory that a progressive destruction of tubercle bacilli is brought about. Also, the fact that the macroscopic lesions are more pronounced in the omentum of the animals with primary infections upholds the same theory.—*Tenure en bacilles de Koch de l'exsudat péritonéal et de l'épiploon des cobaye primo-infectes et surinfectes, A. Gaiginsky & R. Laporte, Comp. Rend. Soc. Biol., November 10, 1934, cxvii, 569.*—(*M. T. W.*)

New Synthesis of Pigment of Tubercle Bacillus, Phthiocol.—2-methyl-3-hydroxy-1, 4-naphthoquinone was obtained in 41 per cent yield by decarboxylating 3-hydroxy-1, 4-naphthoquinone-2-acetic acid. The product thus obtained was identical in properties with phthiocol, the pigment naturally occurring in the human tubercle bacillus.—*The Chemistry of the Lipids of Tubercle Bacilli. XXXVIII. A New Synthesis of Phthiocol, the Pigment of the Human Tubercle Bacillus, M. S. Newman, J. A.*

Crowder & R. J. Anderson, J. Biol. Chem., May, 1934, cv, 279.—(F. B. S.)

Merthiolate and Other Antiseptics for Tubercle Bacilli.—In 1920 Calmette summarized the results obtained by various workers on the effects of various antiseptics on tubercle bacilli, used in relatively concentrated solutions; but the effect of weaker solutions, such as might be employed in preparing bacterial vaccines or therapeutic sera, has received little attention, apart from the studies of Wells, De Witt and coworkers, which was along rather different lines. Merthiolate (sodium-ethyl-mercury-thiosalicylic acid), introduced by Powell and Jamieson in 1931, is now commonly incorporated in certain therapeutic preparations. Therefore, it was desired to test its effects in comparison with those of more commonly used antiseptics, on the viability of tubercle bacilli. The other antiseptics were formalin solution, free from acid and containing 35 per cent formaldehyde, and pure crystalline phenol. The organism used was a bovine strain of *B. tuberculosis*, supplied by Griffith, the final mixture of suspension in salt solution containing 1 mgm. moist tubercle bacilli per cc. together with the various antiseptic solutions, kept at room temperature throughout. After 1, 2, 4, 7, 14 and 28 days respectively, 0.5-cc. quantities were injected into the thigh muscles of white or cream-colored guinea pigs weighing 400 to 500 gm. For the last two tests more concentrated bacillary masses were used (obtained from centrifugating 2.5 cc. quantities of suspension). A control series of 20 guinea pigs was injected with moist bacilli in physiological salt solution. *Results:* All of the controls save one killed for another experiment died and showed generalized tuberculosis at necropsy. Of the remaining 80 animals, 21 died and all but 4 of these showed generalized tuberculosis. The surviving animals were kept under observation a year, at which time their average weight was 720 gm. and all but one appeared healthy. All but one survived an injection of 1 cc. of Old Tuberculin and failed to show any signs of tuberculosis. *Conclusions: 1:* Phenol in 0.5 per cent concentration kills tubercle bacilli in less than twenty-four hours, but 0.25 per cent concentration is much less effective, living bacilli being occasionally demonstrable after fourteen days. *2:* Merthiolate, 0.02 per cent, is lethal in twenty-four hours and in a concentration of 0.01 per cent after four days. *3:* The results with formalin were complicated by the animal which succumbed following injection of Old Tuberculin a year after receiving 2.5 mgm. of tubercle bacilli exposed to 0.1 per cent formalin for fourteen days. The possibility of contact infection cannot be entirely excluded.—*The Effect of Dilute Solutions of Certain Antiseptics on the Viability of Tubercle Bacilli, S. R. Douglas & P. Hartley, Tubercle, December, 1934, xvi, 7.—(A. P.)*

Morphological and Tinctorial Behavior of *B. Leprae.*—The uncontaminated subcutaneous nodules from 4 cases of human leprosy were cultured upon a variety of media including living chick embryo and growing tissue. During a period of observation of six months only minor alterations in the size and shape of the *B. leprae* were noted, similar to what occurs in the case of the tubercle bacillus under like conditions. When multiplication of the lepra bacillus first occurred, the acid-fast rods became longer, thicker, less curved and more distinctly diphtheroid in appearance, because of the bipolar massing of the chromatin. Later, when the organism acquired the power to grow independently of the host's tissue, it became shorter, plumper, and often without granules. When macroscopic growth was well established, the bacilli assumed the morphology of those in the transplanted leprous tissue. Branching and filamentous and interlacing streptothrical forms were never encountered. The carbol-fuchsin-stained microörganism of leprosy is less resistant to decolorization than is the tubercle bacillus, and, if this period of decolorization is shortened, the leprosy bacillus remains deeply stained. Failure to realize this fact may account for the reports of non-acid-fast diphtheroid and streptothrical forms. The macroscopic culture of this Hansen organism of human leprosy, *B. leprae*, was obtained only after months of careful cultivation upon split-protein media, preferably that of the excised, transplanted autolyzing leproma. When once it successfully passed through this transitional period of *in vitro* adaptation, growth took place readily upon the ordinary laboratory nutrients.—*Morphological and Tinctorial Behavior of B. Leprae during its Adaptation to an in Vitro Habitat, C. W. Duval, Proc. Soc. Exper. Biol. & Med., December, 1934, xxxii, 498.—(F. B. S.)*

Acute Toxicity of Ethyl Chaulmoograte.—Purified ethyl chaulmoograte preparations are more toxic than the ethyl esters of the total fatty acids of chaulmoogra oil. Iodization of the ethyl chaulmoograte with 0.5 per cent iodine does not affect the toxicity. Addition of four per cent creosote increases the toxicity, commensurate with the amount of creosote present. The degree of unsaturation is not a reliable index of toxicity. Sodium chaulmoograte, given intra-

venously, causes acute death in rats in doses of 0.1—0.125 gm. per kg. Intensive treatment of leprous human beings with ethyl chaulmoograte may give rise to a sterile tetanus in rare instances, perhaps related to the type of terminal convulsions seen in rats after administration of a single lethal dose.—*Acute Toxicity of Ethyl Chaulmoograte, G. A. Emerson & H. H. Anderson, Proc. Soc. Exper. Biol. & Med., November, 1934, xxxii, 289.*—(*F. B. S.*)

Pathogenic Fungi.—A collection of photographs and microphotographs is shown, illustrating an exhibit at the 1934 meeting of the Massachusetts Medical Society and prepared by the Department of Dermatology, Tufts College and Medical School and Boston City Hospital collaborating with the Department of Cryptogamic Botany at Harvard University. The exhibit was designed (1) to indicate the position of the fungi pathogenic to man in the plant kingdom and their relation to other fungi, and (2) present the common pathogens in their more important aspects of diagnosis and culture. *Classification:* The *Thallophyta* (Thallus plants) have relatively simple and undifferentiated bodies. Their two subdivisions *algae* and *fungi* are distinguished by the presence or absence of chlorophyll. The fungi, lacking it, are either parasitic or saprophytic. The fungi are subdivided into: *1:* Bacteria. *2:* Slime molds (Myxomycetes), small and unimportant saprophytes. *3:* Eumycetes or higher fungi. These are made up of thread-like strands or hyphae, classified according to their mode of sexual spore production. *4:* Phycomycetes or true molds. Their hyphal threads are not cross-partitioned. They include black-bread mold and important blights such as the Irish potato blight of 1845. *5:* Ascomycetes or sac fungi. These produce sexual spores inside a sac cell. They include baking yeasts and the ergot fungus, also chestnut-bark disease. *6:* Club fungi or Basidiomycetes. These bear sexual spores on special club-shaped cells and include corn smut and white pine and wheat rusts, also mushrooms and puffballs, some of which contain virulent poisons. *7:* Imperfect fungi. Produce no perfect sexual spores. They include many forms of fungi, molds and mildews. *Common fungous diseases:* Diagnosis is suggested by the appearance of the lesion and completed by finding or growing the fungus. A drop of 30 per cent potassium hydroxide on a slide covered by a cover-slip, the slide being warmed over a flame, will bring out hyphal threads and spores. To culture, plant bits of tissue or discharge in tubes of Sabouraud's "proof agar" (glucose 4 gm., peptone 1 gm., agar 2 gm., water 100 cc.) and keep at room temperature. Some pathogens are slow-growing and may not appear for three or four weeks. Most pathogens are white or yellowish in color. Green, dark or rapid-growing colonies are usually contaminations. X-ray reproductions of a case of pulmonary moniliasis are included with the views of skin lesions.—*Exhibit of Fungi Pathogenic to Man Shown at the 153rd Anniversary of the Massachusetts Medical Society, J. G. Downing & S. M. Cousins, New England J. M., November 22, 1934, ccxi, 963.*—(*A. P.*)

X-Ray in Tuberculosis.—Serial films are of far more value than one flat film or stereoscopic films, for they aid materially in determining the activity of tuberculous infections. They must, of necessity, be correlated with other findings, as the film shows only the type and extent of the lesion and is suggestive of the duration and degree of activity. Bronchiectasis, having been excluded, ring-shadows must be regarded as cavities. Serial films which show fluid levels of different heights in cavities must be interpreted as demonstrating an active lesion. The process of healing is seen in the X-ray as increased density, with a smaller and more abrupt periphery with or without linear markings, or the original lesion may entirely disappear. Conversely, progressive or reactivated infections usually show an increase in size and, possibly, new foci. Rarefied areas suggestive of cavities may appear and later become one large cavity or several small cavities. Occasionally, changes of this character are hidden by massive areas of disease. Lesions remaining the same over a period of years may be assumed to be arrested. The presence of pulmonary tuberculosis and its progress are usually shown earlier by X-ray than by symptoms or physical signs and the same is true of reactivity.—*The X-ray in the Measurement of Activity in Pulmonary Tuberculosis, O. S. Pettingill, New England J. M., August 9, 1934, ccxi, 240.*—(*R. C. S.*)

Roentgenology of Apex of Lung.—Radiological stereoscopy is of definite value for the study of the pulmonary apices. The pleural domes may be well demonstrated in normal lungs. The pleural domes are actually much deeper than generally assumed by anatomists, not uncommonly extending below the posterior parts of the 2nd ribs and below the posterior regions of the 1st ribs. The assumption of the anatomists that the pulmonary apices and the pleural domes are situated in the superior aperture cannot generally be considered as certain. Typical appearances of the normal stereo-

scopic films of the superimposed 2nd ribs upon the anterior pleural dome shadows are described. The shadow which has been described as the subclavian artery is due to a density of the pleural dome in the region of the apex. The shadow previously assumed as the azygos vein of the azygos lobe is a result of folding of the pleura.—*Die Lungenspitze im Roentgenstereobild, M. Boenniger, Fortschr. Geb. Roentgenstr., August, 1934, i, 2.*—(*F. G. K.*)

Expiratory Roentgenograms.—The roentgenograms of two cases demonstrate the value of the expiratory phase exposure in detecting small pneumothoraces of 100 to 200 cc. On expiration the mantle of air becomes the thickest. Expiratory-phase exposures with the usual inspiratory-phase exposures give valuable information as to the amount of actual inflation and deflation which is taking place in a collapsed lung.—*The Superior Value of the Expiratory Roentgenogram in the Diagnosis of Incomplete Pneumothorax, S. Greenberg, Am. J. Roentgenol. & Rad. Ther., September, 1934, xxxii, 330.*—(*E. M. J.*)

Roentgenographic Interpretation of Pulmonary Tuberculosis.—This is not always the simple matter it is sometimes thought. The infantile or primary type is distinguished from the adult type, probably a reinfection. Association of enlarged hilar lymph nodes with the former is mentioned, as well as the original primary focus, sometimes so minute as to be invisible before calcification. Calcific areas indicative of healed tuberculosis occur in most adult chests. Lymph-node enlargement alone must be differentiated as to aetiological factors. The variation in size of the hilum in the normal child, shown by the Committee on Medical Research of the National Tuberculosis Association, is alluded to. McPhedran's classification of lesions, as parenchymal, tracheobronchial and adolescent, is adopted, the last approaching the adult type in distribution. It is stated that adult type lesions may begin either in the apical or the infraclavicular region, progressing down by bronchial extension or healing by fibrosis, and that apical lesions are rare under the age of 10 years. Pleural thickening may be visualized when the subpleural lymphatics are engorged, as a dense line on profile view. If unaccompanied by parenchymal changes, however, a diagnosis of tuberculosis is unwarranted. *Differential diagnosis:* For the diagnosis of childhood tuberculosis simple hilum enlargement and increased linear markings alone are insufficient. When there has been an acute pulmonary infection sufficient time should be given for acute manifestations to subside. In the adult, definite parenchymatous changes must be present to warrant a diagnosis of clinical tuberculosis, and the effect of such conditions as asthma, bronchitis, dust inhalation and emphysema or variations from the normal markings must be considered. Even parenchymatous lesions may be confusing, such as the appearance of incompletely resolved upper-lobe pneumonia. Primary lower-lobe tuberculosis is rare. On the other hand, secondary malignant tumor may involve the upper lobes, but the lesions are coarser and more sharply defined. Silicosis may be confusing and may coexist with tuberculosis, while actinomycosis may simulate it. Far-advanced tuberculosis is to be distinguished from abscess, though sometimes the latter, especially when due to Friedländer's bacillus, may closely simulate tuberculosis. Bronchiectatic cavities differ in location. Their relations to bronchi may be shown by lipiodol injection. Caseous tuberculous pneumonia must be distinguished from lobar pneumonia, abscess, tumor, massive collapse, and effusion. Fibroid phthisis must be differentiated from chronic interstitial pneumonia and massive collapse, the only other condition in which heart and trachea are drawn toward the affected side. Miliary tuberculosis has to be distinguished from pneumonoconiosis, carcinomatosis, bronchiolitis. Fluoroscopic study may also be helpful.—*Pulmonary Tuberculosis Roentgenologically Considered, A. S. Merrill, New England J. M., November 15, 1934, ccxi, 916.*—(*A. P.*)

Fluoroscopy in Case-Finding.—In the experience of the Medical Division of the Home Office of the Metropolitan Life Insurance Company prior to 1927 it was noted that even relatively large lesions of pulmonary tuberculosis might not produce symptoms or detectable physical signs. After a trial in 1927 had demonstrated the value of fluoroscopy in finding such cases, examination by this means was conducted on a large scale among applicants for employment. Between January, 1928, and December, 1933, 17,765 applicants were examined. About 95 per cent were girls and 5 per cent boys. The average age was 18 years. Lesions were found in 244 cases, or 13.7 per 1000 examined. Through a follow-up service, 75 per cent of the applicants have been reëxamined. The majority were in need of immediate treatment. The number needing treatment is decreasing year by year. The company is not now employing persons with pulmonary tuberculosis. An analysis of 141 cases diagnosed as negative by X-ray film or fluoroscope shows that significant

pulmonary tuberculosis may develop later in the adolescent or adult, and that these cases may be detected by X-ray before symptoms or physical signs develop.— *Value of the Fluoroscope in Pulmonary Tuberculosis Case Finding, H. H. Fellows, Am. J. Pub. Health, February, 1935, xxv, 109.*—(*E. R. L.*)

Quantitative Tuberculin Tests.—Various authors feel that an accurate tuberculin test would assist in determining activity, though others feel that there is no demonstrable relationship between them. The results of the experiment presented are given as a possible addition to present information on this subject. A group of student nurses and a group of women known to have tuberculosis were studied, the intracutaneous test being employed and readings of the reactions made according to the National Tuberculosis Association standards. Because of severe reactions an initial test of 0.1 cc. of a 1:100,000 dilution was used, and subsequent dilutions of 1:20,000, 1:1,000 and 1:100 used when necessary. All persons tested were subjected to careful X-ray and physical examinations. Among the nurses 80.2 per cent of the positive reactors had no demonstrable tuberculous lesion, 17.8 per cent had fibrotic or calcified lesions, and 2 per cent had evidence of active tuberculosis. The results of the tests performed on the tuberculous patients, in whom the dilutions of 1:1,000 and 1:100 were not needed, were considered in relation to symptoms, extent of the process and the degree of activity of the disease. No definite or consistent relationship could be found between these and the tuberculin tests, nor did patients with arrested lesions react to lower dilutions and patients with active infections mostly to high dilutions. The test probably is an index of the degree of allergy in response to a tuberculous infection, and the author feels that it is possible that other studies may demonstrate some effect that hypersensitiveness may have on such an infection. The conclusion reached is that quantitative tests show no relation to inactivity or the degree of activity of a tuberculous lesion.—*An Analysis of the Quantitative Tuberculin Test as an Index of Tuberculous Activity, T. L. Badger & W. K. Meyers, New England J. M., August 9, 1934, ccxi, 241.*—(*R. C. S.*)

Tuberculin Skin Reactions.—Since Pirquet's tuberculin test in 1907, it has become universally used. Its usual method of application is on the site of a scarification with a small sterilized drill or Pirquet borer sufficient to expose the vascular cutis to the tuberculin. Most observers consider an elevated papule with an area of erythema over 5 mm. in diameter to be a positive reaction, read after twenty-four and forty-eight hours. Craig, in 1916, introduced the multiple puncture or tattoo method, corresponding to that of Hill in vaccination against smallpox. In this a new sharp sterile sewing needle is used, held between the first two fingers above and the thumb below, with the point nearly at right angles (?) to the forearm of the patient. Then, held nearly parallel to the skin, the side of the needle is pressed firmly seven to ten times into the skin through a drop of tuberculin in an area of about 5 mm. in diameter. The elasticity of the skin when pressed pulls a fraction of an inch over the needle point and carries the tuberculin into the deeper layers. There should be no bleeding or evidence of trauma. Stewart, in 1927, introduced the single puncture technique, again using a sewing needle and introducing it through the tuberculin into the dermis for about one-quarter of an inch. The reaction is read after twenty-four and forty-eight hours. *Comparison of multiple puncture (Craig) method with scarification (Pirquet) method:* The Craig test was done on 100 children at the Prendergast Preventorium of the Boston Tuberculosis Association, who were contacts and had already shown positive Pirquet reactions prior to admission. The Pirquet was also repeated. The same arm was used and a Mantoux (intracutaneous) test was done at the same time, using 0.1 cc. of a 1–10,000 dilution, or 0.01 mgm. which Happ and Casparis showed practically equivalent to the amount of tuberculin absorbed in the Pirquet. Human tuberculin from the Massachusetts State Department of Health was used. Controls on the opposite arm were done with sterile salt solution in the case of the scarification and multiple-puncture methods. Any reaction showing an area of erythema of 0.5 cm. in diameter, especially if associated with some induration, was considered positive. Most of these occurred within twenty-four hours in the form of a red elevated papule lasting several days and fading about the fifth day. Severe reactions showed vesiculation, marked erythema and induration, and a few lymphangitis, passing away in several weeks instead of days. In 15 cases the scarification (Pirquet) test was negative, but as 11 were positive when repeated more carefully, the negative result was probably due to improper technique (too superficial scarification). Eight of these had been done by a nurse. Multiple-puncture tests by the same nurse were positive. A few premature or transitory reactions were also obtained, reaching a maximum at ten hours and disappearing on the second day. The pro-

portion of severe, slight and moderate reactions was practically the same with the Craig test as in the case of the intracutaneous test, and also the proportion of positives. Compared with scarification, the tattoo method is distinctly less painful and more certain to introduce the tuberculin into the deeper layers of the skin. The size of the reactions averaged less than with the Mantoux method and about the same as with the Pirquet. However, with scarification even an experienced worker often has difficulty in gauging the proper depth because of variation and texture of different skins. The wide variation in reactors on retesting with the Pirquet seems due chiefly to the factor of technique, as Aronson, Heimbeck, Zacks and others using a strictly uniform technique, found less than 1 per cent more reactors on repetition. *Comparison of multiple puncture (Craig) with single puncture (Stewart) method:* This study was made on 75 children at the Prendergast Preventorium, all contacts and previously positive reactors (Pirquet). The intracutaneous test was simultaneously done, together with controls on the opposite arm using the puncture technique. Reactions were read after twenty-four, forty-eight and seventy-two hours. The single- and multiple-puncture methods agreed in 100 per cent of cases. The single puncture reactions were a trifle more pronounced and papular, and a little speedier. It is not clear that either attains quite the accuracy of the Mantoux. *Conclusions: 1:* Both single- and multiple-puncture methods are less painful than scarification. *2:* The technique is simpler. *3:* No special instruments are necessary. . . . an ordinary sewing needle. . . . . *4:* The incidence of too superficial scarification is eliminated. . . . . *5:* There is less traumatic reaction.—*Studies in Tuberculin Reactions: Scarification, Multiple and Single Puncture Technique, E. Friedman & J. B. Hawes, 2nd., New England J. M., September 6, 1934, ccxi, 446.—(A. P.)*

Quantitative Intracutaneous Tuberculin Tests.—Until recently tuberculin hypersensitiveness was thought to indicate increased resistance or immunity to tuberculosis but it is now more accurately regarded as merely a type of protein sensitiveness, a property of the infected subject, or, following Zinsser, "an increased capacity to react. . . . against an antigen released by the disintegration of the bacillus." Willis showed that "allergy" can fade and immunity persist, and Rich that sensitiveness and immunity are separate entities and that necrotic tissue reactions are harmful. It was desired to confirm for man some of these data from animal experiments. For three years Westwater has carried on studies with the intracutaneous test, a better, more sensitive and more precise test than the Pirquet. *Tuberculin reactivity in children:* It has been established that children in known contact with tuberculosis acquire sensitiveness earlier than noncontacts and that the younger the child the more significant a positive reaction. Westwater tested 170 children selected from some 2,000 cases of acute infectious disease admitted to the Park Hospital at Hither Green, London. As between 35 tuberculosis contacts and 60 noncontacts, there was little difference in intensity of reaction, the figures indicating a slightly larger proportion of pronounced positives among the contacts. Considered according to age, the degree of sensitiveness increased slowly up to 4 or 5 years of age, then steadily declined up to 10 years, beyond which data were not available. It may be remarked that in the first four-year period (2 to 5 inclusive) degree of sensitiveness increases while incidence of actual disease falls markedly. After five years both decline, although the proportion of noncontact reactors increases, due to casual incidental contact with tuberculosis. *Tuberculin reactivity in adult phthisis:* At Colindale Hospital, London, the intracutaneous test has been used quantitatively on cases in all stages, subdivided according to type of disease. The results accord with observations elsewhere. Massive disease is associated with low sensitivity, slight lesions usually with the reverse. Exudative types show a higher sensitiveness than those with fibroid lesions. The more recent and active the disease, if not massive, the higher the sensitivity. Among patients getting worse on routine treatment, sensitivity was stationary or diminished, whereas it increased in a large proportion of those improving. On the other hand, 50 per cent treated by pneumothorax showed diminished sensitivity and only 17 per cent increased sensitiveness. Patients with phrenic avulsion showed less marked differences from those on routine treatment. *Summary: 1:* A quantitative method of using the intracutaneous test is described and the fallacies indicated. *2:* In the primary tubercle infection of childhood. . . . sensitivity varies with the activity of the resistance. *3:* In adult phthisis also the degree of sensitivity varies with the activity of the immunity mechanism. *4:* Collapse therapy tends to decrease sensitivity. *5:* Acute excavation. . . . is associated with high allergy, whereas a low allergy is found in cases with old-standing cavities. . . . . *6:* These results suggest that allergy or sensitivity to tubercle protein is

probably a minor factor in the pathology of the disease.—*Allergy in Tuberculosis. The Quantitative Use of the Mantoux Test, J. S. Westwater, Tubercle, September, 1934, xv, 543.*—(*A. P.*)

Intracutaneous Tuberculin Tests in General Hospital.—A total of 397 clinically nontuberculous and 57 clinically tuberculous patients, representing a general hospital population, were examined with the intracutaneous tuberculin test using dilutions of 1 in 10,000, 1 in 1,000, and 1 in 100. Of the 346 clinically nontuberculous patients from the age of 15 upward, 35 per cent were positive after the 1 in 10,000 test, 74 per cent after the 1 in 1000, and 86 per cent after the 1 in 100; thus, 14 per cent were negative, even with the last dilution. Assuming a well-defined raised area of erythema, 10 mm. in diameter, as the lowest limit of a positive reaction, 12 per cent of all the readings at 48 hours were doubtful. About two-thirds of these became positive, either at 96 hours or with the next stronger dilution, one-third being negative with the latter. It appears therefore advisable to regard a raised erythematous area at least 10 mm. in diameter as the lowest limit of a positive reaction (rather than merely an erythematous area 5 mm. in diameter) and to consider any less well-defined reaction as doubtful. Eighteen per cent of doubtful and 3.5 per cent of negative reactions at 48 hours became positive at 96 hours. It is suggested that, whenever possible, a patient should first be tested with a dilution of 1 in 10,000 (four patients clinically nontuberculous in this series presented severe local reactions) and the reading be taken at 48 hours. If negative, the test should be repeated with the dilution of 1 in 1,000 the same day, but if doubtful this should be postponed until a further reading has been made at 96 hours. A similar procedure should be adopted after the test with 1 in 1,000 dilution. After the 1 in 100 test all doubtful and negative reactions should be read again after 96 hours. The syringe is described and illustrated. It is claimed that its use is simple and rapid, and accuracy of dosage is assured. It is useful for applying the Mantoux test to infants.—*The Mantoux Test in a General Hospital Population, with a Note on the Intradermal Syringe of Pictet, G. G. Kayne, Lancet, December 15, 1934, ccxxvii, 1333.*—(*B. T. McM.*)

Value of Sputum Cultures.—An investigation was carried out to determine whether culturing sputum on the Bordet-Gengou and the Loewenstein media could be safely substituted for inoculation into guinea pigs in detecting small numbers of tubercle bacilli. Two hundred and thirty-three sputa from 181 patients were used in the test. These were negative microscopically even after digestion with sodium hydroxide or oxalic acid. One half of the sediment from each sputum was cultured on both media and the remaining half was inoculated into 2 guinea pigs. Unfortunately, the first 123 specimens were collected in nonsterile cups; hence the cultures were often contaminated with spores and molds, and a large number of guinea pigs died of other infections too soon to be examined for tuberculosis. The subsequent specimens were collected in sterilized containers and the results were more satisfactory. Only 4 sputa were lost through contamination in the second series; but the guinea pigs inoculated with thirty-four of the specimens died too soon to show tuberculous lesions. Combining both series, 22 sputa were found positive on culture or inoculation into guinea pigs. Eighteen were positive on the Bordet-Gengou medium, 13 on Loewenstein's medium, and 15 were positive on animal inoculation. In 4 sputa, all except one of the animals were dead in 12 days and were reported free from tuberculosis on autopsy. They died before it would be possible to recognize tuberculosis in them. The corresponding cultures were all positive. Hence, the experiment is really limited to a comparison of media and not to culture versus inoculation. The authors conclude that the cultivation of sputum is a successful substitute for inoculation into guinea pigs to detect rare bacilli and they believe that the Bordet-Gengou medium is one of the best for this purpose. This consists of glycerin-potato-agar, which, when needed, is melted, cooled and mixed with one-third of its volume of sterile normal blood.—*Bordet-Gengou and Löwenstein Mediums in Detecting Tubercle Bacilli in Sputum, L. Mishulow, M. Romano, M. Melman & C. Kereszturi, J. Infect. Dis., November-December, 1934, lv, 402.*—(*J. S. W.*)

Guinea-Pig Inoculation.—After studying two series of 400 pairs of guinea pigs each, the method used is recommended as a routine procedure in suspected cases which do not show tubercle bacilli on direct smear. The technique is as follows: The clinical material is first centrifugated for one hour at 2500 *r.p.m.* in a centrifuge with a head-radius of 13.5 cm. One cc. at the top is pipetted off and, with enough physiological salt solution to make 5 cc., is added to the sediment. The 5 cc. is injected into 2 guinea pigs, one intraperitoneally and the other subcutaneously. If the guinea pig dies before three weeks and no gross tuberculous lesions are evident, the test is considered a

failure. The same after three or more weeks is considered a negative test. If both animals are alive at four weeks the one receiving the intraperitoneal injection now receives 0.5 cc. of Old Tuberculin subcutaneously. If it dies and is found to be tuberculous the mate is killed and examined. Usually only gross examination is necessary. When tuberculin tested, three-fourths of the infected animals will die within forty-eight hours, and the chances are only one to thirty that those surviving the tuberculin infection will show tuberculosis at the end of eight weeks. Thus the animal inoculation diagnosis of tuberculosis is shortened by three weeks and is more accurate than the culture method.—*Large Doses of Tuberculin in Testing Guinea Pigs Inoculated for Diagnostic Purposes, T. B. Magath, Am. J. Med. Sc., September, 1934, clxxxviii, 403.*—*(E. M. J.)*

Active Pulmonary Tuberculosis.—For seven years the Metropolitan Life Insurance Company has conducted very careful examinations of employees at the time of application for positions, and annually thereafter. During this time 141 were found to be tuberculous. A careful history was taken and the physical examination was not considered complete without roentgenoscopy. If any suggestive data were elicited, a roentgenogram and sputum examinations were made. The reasons for taking the roentgenogram on which the diagnosis was made were history in 73 cases, fluoroscopic findings 59, routine re-roentgenogram 9. The large majority of the 141 were 17 to 24, but 27 were over 25 years of age. Sixty-five per cent had minimal; 30 per cent moderately advanced; and 5 per cent far-advanced tuberculosis. Sixty-five per cent were symptom-free or had only one symptom, not in itself pathognomonic. Only 42 per cent had râles and 4 per cent evidence of pleurisy with effusion. Loss of weight was not a significant factor and was not greater in the moderately and far-advanced cases. In 31 per cent tubercle bacilli were found in the sputum on direct smear or animal inoculation either at the time of diagnosis or during their subsequent treatment. Thirty-eight per cent of those diagnosed from suggestive history had positive sputum as compared with 19 per cent of the group having only positive roentgenoscopic finding on routine re-examination. It is possible to detect cases of active pulmonary tuberculosis roentgenologically before symptoms and physical signs become established.—*Significant Active Pulmonary Tuberculosis in the Apparently Healthy Adult. A Study of 141 Cases, H. H. Fellows, Am. J. Med. Sc., October, 1934, clxxxviii, 533.*—*(E. M. J.)*

Leucocytes and Activity in Pulmonary Tuberculosis.—Kaminsky states (quoting Medlar) that, when the neutrophiles are above 5000 per cmm., tuberculous lesions are undergoing abscess-formation or ulcerating lesions are extending. With monocytes above 700, there is evidences of new tubercle-formation; and, with lymphocytes above 2000, progressive healing. In the septic leucocyte picture, neutrophiles are above 65 to 75 per cent, and lymphocytes below 20 to 25 per cent. It is stated that septic leucocyte pictures persist as long as there are clinical indications for rest and often beyond that, and that with arrest established the picture becomes nonseptic. This series of counts was on 356 consecutive admissions to Middlesex County Sanatorium, Waltham, Massachusetts. It is stated that when there is a discrepancy between the blood picture on the one hand and the clinical and roentgenographic findings on the other, the former should be regarded as the more reliable index of activity. Some individual graphs are included.—*The Leucocytic Picture as an Aid in the Measurement of Activity in Pulmonary Tuberculosis, J. Kaminsky, New England J. M., August 9, 1934, ccxi, 245.*—*(A. P.)*

Schilling Differential and Red-Cell Sedimentation as Indices of Tuberculous Activity.—A distinction is made between clinical and pathological activity in tuberculosis. It now seems accepted that erythrocyte sedimentation is dependent on cellular destruction and its rate directly proportionate to the amount. It is found increased in all cases of increased protein catabolism and bears a significant relation to plasma fibrinogen content. It is independent of changes in the white blood cells. Anaemia affects the sedimentation rate. Normal sedimentation is practically never found in clinically active tuberculosis. Schilling's classification of the neutrophilic leucocytes led to counting of the various types he describes. He found an increase in immature cell types usual in tuberculosis, and especially of the "juveniles" in severe infections. The present data were from 35 female patients at the Channing Home, Boston. Standard technique, using the Wright stain, was employed, also the haematocrit and sedimentation determined and the rate corrected for variations. The blood-curves obtained were found generally to parallel the clinical picture but abnormal findings persisted long after clinical symptoms. It is not assumed that, therefore, all patients should be regarded as invalids until normal curves are obtained, yet caution is suggested. As all minimal cases had definitely abnormal blood pictures, an aid

to diagnosis seems promised.—*The Schilling Differential Count and Red Cell Sedimentation Rate as a Measurement of Activity in Pulmonary Tuberculosis, J. W. Cass & M. Sutermeister, New England J. M., August 9, 1934, ccxi, 252.*—(*A. P.*)

Monocyte-Lymphocyte Ratio and Activity in Pulmonary Tuberculosis.—This study is based on blood counts of 800 consecutive admissions to Rutland State Sanatorium (Massachusetts), correlated with independent clinical findings and estimate of the cases. The ratio has also been correlated with subsequent results. Supravital staining was not used, as being too time-consuming and complicated for routine work. Among the 800 consecutive admissions were 730 cases of pulmonary tuberculosis, 13 of childhood type, 7 of pleurisy with effusion, and 50 nontuberculous cases. Most of the childhood type and the nontuberculous had a normal monocyte-lymphocyte ratio. In pleurisy with effusion, on the other hand, the ratio was uniformly high. *Correlation to state of disease:* Many minimal or stage-I cases had a normal or nearly normal ratio and none showed a ratio over 0.9 (normal being considered 0.3). The more advanced the disease the higher the general trend of the ratio, with, however, considerable variation. *Correlation with prognosis:* The clinical estimate, represented by the consensus of opinion of the majority of the staff, while often coinciding with the trend of the monocyte-lymphocyte ratio, proved in other cases more reliable when the two diverged. *Correlation with results under observation:* Of 111 with a normal ratio, 88.2 per cent improved. As the percentage of improved decreased the monocyte-lymphocyte ratio increased. Also, 16 with a ratio of 1.0 or over improved, indicating that a pessimistic view based on a high ratio is not always justified, though the event is to be viewed with concern. Successful active therapy, of course, may bring about a rapid change. On the other hand, 25 per cent with a ratio of 1.0 or over were dead within three months. *Summary and conclusions:* The monocyte-lymphocyte ratios of 730 patients on admission (with pulmonary tuberculosis) represent the various ratios that might be obtained in one individual in the course of his disease. The ratio cannot, therefore, be regarded as a diagnostic criterion. In the group with normal or nearly normal ratio, many were definitely active, as indicated by toxic clinical phenomena, and many showed increased sedimentation and a shift to the left in the polymorphonuclear differential. The monocyte-lymphocyte ratio, therefore, is not a sensitive index of activity. It does indeed furnish a valuable indication of how the individual is handling his infection, an increasing ratio indicating a losing fight, a decreasing one the reverse. It is thus of value prognostically and constitutes an objective fact which ought to be more widely utilized.—*The Monocyte-Lymphocyte Ratio as a Measurement of Activity in Pulmonary Tuberculosis, G. L. Muller & D. Davidson, New England J. M., August 9, 1934, ccxi, 248.*—(*A. P.*)

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